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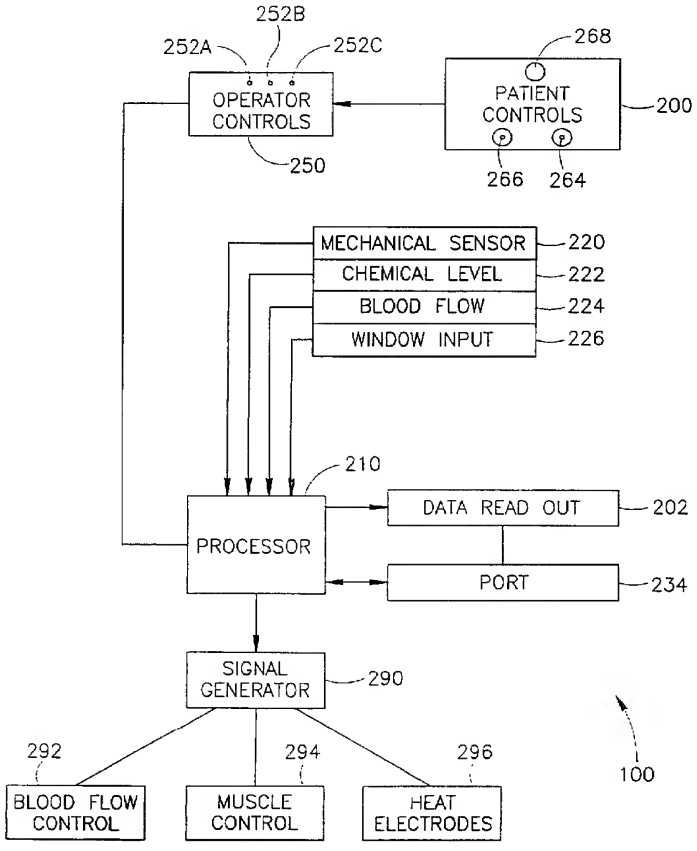
(54) Title: BLOOD FLOW CONTROLLER



(57) Abstract: A method of treating a tissue condition by electrifying a selected blood vessel with an electric field (292) that modifies blood flow associated with a treated tissue by directly acting on the blood vessel, receiving an automatic indication (224) of a local effect of electrification, and varying the electrification responsive to the indication.

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BLOOD FLOW CONTROLLER

RELATED APPLICATIONS

This application claims the benefit under 119(e) of US provisional application 60/177,436, filed January 21, 2000 and US provisional application 60/252,345, filed December 21, 2000. This application is also related to PCT applications PCT/IL00/00319, PCT/IL00/00832, PCT/IL00/00837, PCT/IL00/00566 and PCT/IL00/00132. This application is also related to a US application filed on December 11, 2000, with a local attorney docket 39046, titled "Acute and chronic electrical signal therapy for Obesity" and invented by Shai Policker et al. The disclosures of all of the above applications are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention is related to the field of controlling blood flow using electric fields.

BACKGROUND OF THE INVENTION

The use of locally applied electrical fields for increasing blood flow is described, for example, in "Electrical Field Stimulation - Meditated Relaxation of a Rabbit Middle Cerebral Artery", D.A. Van Ripper and J. A. Bevan, Circulatory Research 1992; 70:1104-1112, the disclosure of which is incorporated herein by reference, which describes causing the relaxation of an artery by applying an electric field.

PCT application PCT/IL97/00243, the disclosure of which is incorporated herein by reference, describes controlling blood pressure in a person by selectively relaxing and contracting large blood vessels in the body using electric fields.

SU 1147408, the disclosure of which is incorporated herein by reference, describes applying an electric field to a blood vessel to prevent blood pooling in the spleen.

In various known treatment methods, blood flow to a body part is modified by a number of methods, including medication, exercise and heating.

SUMMARY OF THE INVENTION

An aspect of some embodiments of the present invention relates to modifying blood flow to peripheral tissue by applying an electrical field. In an exemplary embodiment of the invention, the blood flow is increased to denuded tissue such as a diabetics-related ulcer. Optionally, a feedback mechanism is used to control the electric field application. In an exemplary embodiment of the invention, the use of a feedback

mechanism allows a reduction in total field applied and/or allows a more effective application of electricity. In an exemplary embodiment of the invention, peripheral tissue is tissue within 1 or 2 cm from the skin and/or within 10 or 20 cm from the ends of appendages.

In an exemplary embodiment of the invention, the electric field is applied to have the effect of relaxing arteries leading to a targeted area, so that incoming blood flow is increased. Alternatively or additionally, the electric field is applied so that it increases capillary perfusion at or near the treated area, possibly indirectly causing an increase in blood supply via the leading arteries. Alternatively or additionally, the electric field is applied to relax veins and/or muscles constraining the veins leading from the treated area, thus allowing better blood evacuation. Alternatively or additionally, the muscle tone of the veins and/or surrounding muscles is increased, so that venous pumping action is enhanced.

Alternatively or additionally to affecting blood supply, the electric field may directly assist in the provision of nutrients from the blood flow to the treated tissue. In an exemplary embodiment of the invention, the electric field opens pores or channels in the tissue separating the denuded tissue from the blood vessels (e.g., a basement membrane). Alternatively or additionally, the electric field applies an iontoporesis force on the nutrients, to aid its migration into the treated tissue.

Optionally, the same (or a different) electric field also provides medication to the treated tissue, for example medication and/or nutrients provided from outside the body or from the blood flow.

Optionally, the application of the field is synchronized to the blood pressure pulse arrival at the tissue.

Optionally, the electric field is sub-threshold, in that it is not sensed by the patient and/or does not cause contraction of nearby skeletal muscles. In some case, no sensory stimulation is allowed. In others, some stimulation is allowed, but not pain sensations.

The electric field may be applied continuously or periodically, with the same field or a different field being applied at different repetitions. The periodicy may be determined ahead of time or it may be varying, for example, manually or automatically. The time scale of the repetitions may be, for example, seconds, minutes, hours or days.

In some embodiments of the invention, one or more parameters of the electric field may vary in time or space. In an exemplary embodiment of the invention, such variation is

useful for providing a certain treatment protocol for a tissue and/or disease state and/or for preventing attenuation or conditioning of the tissue response.

An exemplary application for such variation of electric field is in Reynaud's Phenomenon or Disease where electric induction is used to counteract an inappropriate reaction to cold. Variation of the electric induction voltage, frequency, amplitude, periodicity and/or envelope, for example, can ensure an appropriate therapy for varying amounts of cold in the environment and can prevent the targeted tissues from becoming conditioned and failing to respond to specific electric field factors.

The electric field may be applied to the treated tissue, near the treated tissue and/or to remotely located tissue, for example, to prevent negative side effects of the treatment or the disease. The electric fields may be applied to multiple points or areas, with different field effects being achieved by the same or different electrodes.

In an exemplary embodiment of the invention, the electric field is applied using electrodes that are integrated in a garment or halter, for example, a stocking that covers the targeted tissue of the foot, a glove that covers the targeted tissue hand or in a halter that covers the targeted tissue of the chest.

An aspect of some embodiments of the invention relates to controlling flow of blood, nutrients and/or medication to a tissue by applying an electric field and using an artificial feedback mechanism to control the electric field. In an exemplary embodiment of the invention, the electric field and the feedback mechanism replace, counteract or supplement an existing, possibly faulty bodily feedback mechanism, for example, a body feedback mechanism that is causing or maintaining a disease state. Alternatively or additionally, the artificial feedback mechanism is designed to prevent or counteract adverse effects of the treatment or of the disease state.

In an exemplary embodiment of the invention, the feedback measures a local parameter, for example local perfusion, rather than a systemic parameter as in other embodiments, for example a vascular parameter such as blood pressure or a non-vascular parameter such as body temperature or glucose level.

In an exemplary embodiment of the invention, the feedback is based on objective sensing of one or more variables. In an exemplary embodiment of the invention, the sensed variable is the controlled flow, for example, blood volume, nutrient flow or medication availability. Alternatively or additionally, the sensed variable is an effect of the

controlled flow (or a material carried by the flow, such as medication), for example, pooling of blood, wetness or pH at denuded tissue and/or temperature of the treated tissue. The sensing may be at the treated tissue, at adjacent tissue or at a remote tissue affected by the treated tissue or the treatment. Alternatively or additionally, sensing is performed on a healthy tissue, to assist in determining a desired state for the treated tissue and or to prevent damage to healthy tissue (e.g., determining allowed ranges in healthy non-treated tissue).

Alternatively or additionally, the sensed variable is an environmental variable, for example an external temperature or humidity level.

In an exemplary embodiment of the invention, the electric field (and optionally its response to feedback) is applied using a protocol designed to heal the diseased tissue. Alternatively or additionally, the protocol prevents further degradation.

In an exemplary embodiment of the invention, the electric field is applied in conjunction with other therapy. Optionally, at least one of the electric field therapy, the other therapy and the feedback protocol are designed and/or modified to work together. The electric field therapy and the other therapy, may be applied at a same time or not, for example, at markedly different times or one therapy after another therapy. One or both therapies may be sporadically, periodically or continuously applied. An exemplary other therapy is the smooth muscle control, for example of the GI tract or the uterus, as described in the above PCT application PCT/IL97/00243.

In an exemplary embodiment of the invention, a nelectric field application is used to increase tissue tolerance to the other therapy. For example, increasing blood flow using electric fields can allow increased levels of therapy without oxygen privation.

Alternatively or additionally, the electric field counteracts or prevents a negative effect of the other therapy, for example increasing blood flow to prevent undesired hyperthermia in heat treatments or to prevent localized constriction of blood vessels in therapy that constricts blood vessels all over the body.

Alternatively or additionally, the therapy, for example, medication, counteracts or prevents a negative effect of the electric therapy.

Alternatively or additionally, the electric therapy and the other therapy have a synergistic therapeutic interaction.

Optionally, a feedback sensor is used to assess the effect of the other therapy, for example, to assist in determining how often, what type, what degree and what amount of other therapy is beneficial.

An aspect of some embodiments of the invention relates to regulating blood flow between organs and within organs to different parts thereof. Optionally, the regulation uses a feedback mechanism to determine and/or regulate various effects of the blood flow regulation. Alternatively or additionally, the regulation is synchronized with another therapy being applied to the organ, for example, electrical control of the organ function.

In an exemplary embodiment of the invention, electrical control of vessels in an organ is used to reduce or increase blood flow to part of the organ. In some organs, such as the penis, a sequence of relaxation/tensioning may be required to assure that blood reaches all the parts of the organ in a desired manner.

Alternatively or additionally, blood flow to an organ is reduced to kill or stunt a portion of tissue, such as fat cells or a tumor.

Alternatively or additionally, blood flow to an organ is increased to wash away material from the organ or to increase the organ's throughput.

There is thus provided in accordance with an exemplary embodiment of the invention, a method of treating tissue with a problem of reduced nutrient availability, comprising:

selecting at least one blood vessel associated with a peripheral body tissue having a reduced nutrient availability;

selecting a location adjacent said selected blood vessel; and

electrifying said selected blood vessel from said location with an electric field that modifies blood flow associated with said tissue by directly acting on said blood vessel,

wherein said tissue comprises peripheral body tissue.

In an exemplary embodiment of the invention, said blood vessel comprises an artery. Alternatively or additionally, said blood vessel comprises a vein. Alternatively or additionally, said blood vessel comprises a capillary bed.

In an exemplary embodiment of the invention, said location is on said treated tissue. Alternatively, said location is adjacent said treated tissue. Alternatively, said location is remote from said treated tissue.

In an exemplary embodiment of the invention, said electrification increases blood

flow to said treated tissue. Alternatively or additionally, said electrification increases drainage from said tissue.

In an exemplary embodiment of the invention, said electrification is timed relative to a motion of an organ associated with said treated tissue. Optionally, said organ comprises an appendage.

In an exemplary embodiment of the invention, said electrification is timed relative to an arrival of a pulse wave at the treated tissue or the location.

In an exemplary embodiment of the invention, the method comprises periodically repeating said electrification. Optionally, said repeated electrifications are the same. Alternatievly, said repeated electrifications have at least one changed parameter.

In an exemplary embodiment of the invention, said selecting comprises selecting a vessel associated with ulcerous tissue. Alternatively or additionally, said selecting comprises selecting a vessel associated with pre-ulcerous tissue.

In an exemplary embodiment of the invention, the method comprises locally providing a molecule to said ulcer. Optionally, said provision is assisted by said electrification.

In an exemplary embodiment of the invention, selecting comprises selecting a single blood vessel. Alternatively, selecting comprises selecting multiple blood vessels.

In an exemplary embodiment of the invention, the method comprises:

receiving an indication of an ambient environmental condition; and

applying said electrification responsive to said indication.

Alternatively or additionally, the method comprises:

receiving an indication of an effect of said electrification; and

varying said electrification responsive to said indication. Optionally, said effect comprises a change in blood flow. Alternatively or additionally, said effect comprises a therapeutic effect of said electrification. Alternatively or additionally, said effect comprises an adverse effect of said electrification.

In an exemplary embodiment of the invention, said treated tissue comprises diabetes-mellitus affected tissue. Alternatively or additionally, said treated tissue comprises Raynaurd's-disease affected tissue. Alternatively or additionally, said treated tissue comprises pressure sore tissue.

In an exemplary embodiment of the invention, said varying reduces an effect of

said field. Alternatively or additionally, said varying stops an effect of said field. Alternatively or additionally, said varying reverses an effect of said field.

There is also provided in accordance with an exemplary embodiment of the invention, a method of treating a tissue condition, comprising:

electrifying a selected blood vessel with an electric field that modifies blood flow associated with a treated tissue by directly acting on said blood vessel,

receiving an automatic indication of a local effect of said electrification; and

varying said electrification responsive to said indication.

Optionally, said effect comprises a change in blood flow. Alternatively or additionally, said effect comprises an increase in blood flow. Alternatively or additionally, said effect comprises a therapeutic effect of said electrification. Optionally, said therapeutic effect comprises an increase in an activity of said tissue. Alternatively or additionally, said therapeutic effect comprises a reduction in an activity of said tissue.

In an exemplary embodiment of the invention, said therapeutic effect comprises a modification of a molecule level in said tissue. Optionally, said molecule comprises a nutrient. Alternatively or additionally, said molecule comprises a medication level in said tissue. Alternatively or additionally, said molecule comprises a toxic molecule. Alternatively or additionally, said molecule comprises a hormone.

In an exemplary embodiment of the invention, said modification comprises an increase in the molecule level. Alternatively or additionally, said modification comprises a decrease in the molecule level.

In an exemplary embodiment of the invention, said effect comprises an adverse effect of said electrification. Optionally, said adverse effect comprises blood pooling.

In an exemplary embodiment of the invention, varying comprises further increasing said blood flow. Alternatively or additionally, varying comprises reducing said blood flow.

In an exemplary embodiment of the invention, the method comprises receiving a manually assisted indication of a physiological parameter and wherein said varying is responsive to said manually assisted input.

In an exemplary embodiment of the invention, the method comprises receiving an indication of an environmental variable and wherein said varying is responsive to said environmental variable.

In an exemplary embodiment of the invention, said electrification is synchronized to a physiological parameter. Alternatively or additionally, said electrification is synchronized to a user input. Alternatively or additionally, said electrification is synchronized to another therapy associated with said treated tissue. Optionally, said electrification prevents or counteracts an adverse reaction caused by said other therapy. Alternatively or additionally, said electrification enhances said other therapy. Alternatively or additionally, said other therapy counteracts or prevents an adverse effect of said electrification. Alternatively or additionally, said other therapy comprises a medication-based therapy. Alternatively or additionally, said other therapy comprises a heat therapy. Alternatively or additionally, said other therapy comprises an exercise therapy. Alternatively or additionally, said other therapy comprises electrical control or activation of muscles.

In an exemplary embodiment of the invention, said tissue comprises skin. Alternatively, said tissue comprises an internal organ. Optionally, said internal organ is selected from the group comprises kidney, liver, pancreas, gall bladder, brain and GI tract. Alternatively or additionally, said electrification redistributes blood within said organ such that two parts of said organ have different blood flow levels. Alternatively or additionally, said electrification redistributes blood between two organs. Optionally, said two organs do not share a secondary supply vessel.

In an exemplary embodiment of the invention, said tissue comprises adipose tissue. Alternatively, said tissue comprises a tumor.

There is also provide din accordance with an exemplary embodiment of the invention, apparatus for treating using vascular control, comprising:

an electric field applicator adapted to apply an electric field to a blood vessel;

a sensor for detecting an effect of said applied electric field; and

a controller that varies said field application responsive to said detected effect.

BRIEF DESCRIPTION OF THE FIGURES

Non-limiting embodiments of the invention will be described with reference to the following description of exemplary embodiments, in conjunction with the figures. The figures are generally not shown to scale and any measurements are only meant to be exemplary and not necessarily limiting. In the figures, identical structures, elements or parts which appear in more than one figure are preferably labeled with a same or similar

number in all the figures in which they appear, in which:

Fig. 1 is a schematic illustration showing a flow controller attached to an ulcerous leg, in accordance with an exemplary embodiment of the invention;

Fig. 2 is a schematic block diagram of a controller according to Fig. 1;

Fig. 3 is a schematic diagram showing the use of a flow controller for an internal organ, in accordance with an exemplary embodiment of the invention;

Fig. 4 is a showing of an exemplary control box for a flow controller in accordance with an exemplary embodiment of the invention;

Figs. 5A-5E show exemplary electrode designs in accordance with exemplary embodiments of the invention;

Figs. 6A-6B show exemplary electrification wave forms in accordance with exemplary embodiments of the invention;

Figs. 7A-7C show exemplary electrode halter arrangements in accordance with exemplary embodiments of the invention;

Fig. 8A is a flowchart of an exemplary process of using a controller, in accordance with an exemplary embodiment of the invention;

Fig. 8B is a flowchart of a method of calibrating a controller in accordance with an exemplary embodiment of the invention; and

Figs. 9A-13B illustrate schematic diagrams of experimental set ups and experimental results, used to determine exemplary pulse parameters.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

EXEMPLARY CONFIGURATION FOR ULCERS

Fig. 1 is a schematic illustration showing a flow controller 100 attached to an ulcerous leg 170, in accordance with an exemplary embodiment of the invention. In an exemplary embodiment of the invention, controller 100 comprises a control box 120 and one or more electrodes, such as electrodes 104 and 102. In an exemplary embodiment of the invention, control box 120 is removably attached to leg 170, for example, by a strap 108. However, other attachment methods, as well as implantable controllers will be described below.

In the exemplary configuration shown, electrodes 104 and 102 are positioned around an ulcer 110 here shown over an ankle 112. Often, ulcers are caused or do not heal well due to reduced blood flow and/or nutrient flow to the tissue surrounding the ulcer. In

an exemplary embodiment of the invention, electrode 104 is designed to increase the blood flow to the ulcer. 110. In an exemplary embodiment of the invention, the flow is increased by the electrode applying an electric field to relax blood vessels at or about ulcer 110. Exemplary useful pulses for effecting vessel relaxation and methods or determining such pulses are described below.

An optional mesh electrode 102 is provided, for example, for increasing the flow of nutrients to the ulcer 110 in a manner that will be described further on. Other electrode types, locations and functions may be useful, some of which will be described below.

In some exemplary embodiments of the invention, controller 100 includes a feedback mechanism for regulating the degree of flow increase and/or other parameters thereof.

In an exemplary embodiment of the invention, an optional sensor 136 determines the blood flow to a digit 140, which can indicate an effect of the flow increasing electric field on the flow to the foot as a whole. Alternatively, a sensor may be placed nearer to ulcer 110.

In an exemplary embodiment of the invention, flow to the ulcer and/or the foot as a whole are increased using one or more electrodes placed remote from the ulcer, for example, a pair of optional electrodes 150 and 152 located adjacent an artery or a sympathetic nerve leading to the foot. Alternatively or additionally, electrodes 150 and 152 are used for providing an alternative stimulation that will be explained below.

Alternatively or additionally to providing feedback on blood flow to the ulcer, feedback may be provided on a negative effect of the electric field or the ulcer, for example using an optional sensor 132. In one example, sensor 132 is used to detect venous pooling of blood caused by increase in blood flow to the foot beyond the venous return capability in the particular patient. Thus, in some embodiments of the invention, controller 100 will stop increasing blood flow or even reduce blood flow, if required, for example by applying an electric field to constrict arteries leading to the treated area..

The placement and shape of the various electrodes, 102 and 104 and sensors 132, 136 can be varied according to the shape of the ulcer 110 or desired effect. These and other factors will be described below.

OVERVIEW OF DEVICE COMPONENTS

Fig. 2 is a schematic block diagram of an exemplary implementation of flow

controller 100. In an exemplary embodiment of the invention, controller 100 comprises a signal generator 290 which electrifies one or more electrodes, for example, blood flow control electrodes 292. In an exemplary embodiment of the invention, controller 100 includes a processor 210 for controlling signal generator 290 and optionally receiving and/or processing feedback signals from various sensors. Alternatively or additionally, other electrodes are controlled by signal generator 290 and/or processor 210 as well, for example, optional muscle control electrodes 294 and/or optional heating electrodes 296. Alternatively or additionally, other therapies may be provided and/or coordinated by processor 210.

In an exemplary embodiment of the invention, signal generator 290 and processor 210, as well as various controls and input/output ports described below are integrated into control box 120. Alternatively, some components of controller 100 may be provided separately, for example, using wired or wireless connections. Other packaging options are described below.

In an exemplary embodiment of the invention, controller 100 includes a user input, for example one or more knobs 264 and 266. Such inputs may be used, for example, for allowing a user to set the device operational parameters, turn the device on or off or provide subjective indications to the device. Alternatively or additionally, such inputs may be used by an operator, for example, for programming the device, for selecting between programs (e.g., based on patient medication schedule or disease state) and/or for entering objective feedback. Optionally, a separate operator control unit 250 is provided, which can be selectively attached to controller 100, and includes for example controls 252a-252c. A separate user input/output box 200 may be similarly provided.

Alternatively or additionally, controller 100 may provide an output to a user, for example, generating an alert based on device state (e.g., when the device is malfunctioning) or treatment issues (e.g., when an adverse reaction is detected). Exemplary possible outputs include a display, a LED 268 or an audio (optionally speech) output unit.

Alternatively or additionally, to user input, computer input and output may be provided, for example via computer or telephone ports 202 and/or 234. Such ports may be useful, for example, for one or more of programming, remote access and transmission of alerts to a remote operational facility or operator. Alternatively or additionally to a port,

controller 100 may include a communication device, for example a cellular telephone.

As noted above, in some embodiments of the invention, controller 100 uses automated feedback to control the electrification. Such feedback includes, for example, measurements of one or more parameters of the patient or of the environment. In an exemplary embodiment of the invention, controller 100 includes one or more sensors, for example a mechanical sensor 220, a chemical level sensor 222 and/or a blood parameter sensor 224. Optionally, one or more of these sensors is embodied in the electrodes used for electrification and/or otherwise packaged with the electrodes.

Alternatively or additionally, controller 100 includes a window input 226 for receiving feedback from manually operated sensors, such as dipsticks, that provide a visual indication. For example, a blood glucose level may be indicated to controller 100 by placing a dip-stick with a suitable reagent, that has been dipped in blood next to window input 226, where it can be read by a suitable optical detector.

INTERNAL ORGAN BLOOD FLOW CONTROL

Fig. 3 is a schematic diagram showing the use of a flow controller 300 for controlling the flow to or within an internal organ 302, in accordance with an exemplary embodiment of the invention.

In an exemplary embodiment of the invention, controller 300 is used to increase or reduce blood flow to organ 302. Alternatively or additionally, controller 300 regulates the flow to parts of organ 302.

In the example shown, vessel organ 302 is feed by a supply vein 304, a supply artery 306 and, in some organs, a body conduit or blood vessel 308 for supplying a substrate that is processed by the organ (e.g., blood in the heart and bile in the gall bladder). Alternatively or additionally, an output conduit, such as a urethra may be relaxed or contracted by applying an electric field to the conduit or to surrounding tissue. In one example the organ is a kidney. Many organs, such as the brain, do not have a separate substrate supply vessel 308. In an exemplary embodiment of the invention, one or more of the vessels (blood or non-blood conduits) are relaxed and/or contracted using an electric field, for example that provided by electrodes 310, electrodes 312 and electrodes 314. In applications that utilize feedback, the electrodes themselves may serve as sensors for detecting the degree of relaxation/constriction, the effect on blood flow or the (electrical) activity of the organ. Alternatively a separate sensor is provided, for example a sensor 316

on a supply vessel (or on an output conduit, such as a urethra) and/or a sensor 322 on organ 302 itself. Such a separate sensor may also be used to merely monitor the input rate, without affecting the input, and optionally affecting the blood flow to the organ in response to the input rate.

Alternatively or additionally, to controlling blood flow to or from an organ, flow within an organ (e.g., absolute or relative) may be regulated. For example, one or more electrodes 320 may be used to increase flow to a first portion of organ 302, and one or more electrodes 318 may be used to reduce flow to a second portion of organ 302.

In an exemplary embodiment of the invention, flow to an organ is increased for an implanted organ, indicated by suture points 324, or another organ with reduced function. Such an increase may be used to ensure that sufficient blood flow is provided to the organ while it is being received (or healing) by the body. Such an increase may be provided in addition to electrical control of the organ (or a muscle cell) to reduce its activity and/or enhance provision of medication to the organ. Optionally, the medication delivery is targeted to the organ in question. Alternatively or additionally, blood flow within an organ may be regulated to allow a damaged part to rest and/or have an increased blood supply. Alternatively or additionally, blood flow within an organ is modified to either wash away local concentrations of materials, such as nutrients, toxins, medications or hormones, or to leave them in the organ. Examples of organs which may be controlled include the liver, the kidneys and the spleen.

Additional possible use of blood flow regulation include reduction in growth of kidney and gall stones (e.g., by reducing the secretions of surrounding tissue, by reducing their activity), enhancing or preventing removal of chemicals bound to receptors, for example in the brain, increasing oxygen provision to locations of anaerobic infections, preventing or reducing inflammation, by targeted increase in flow to the damaged area and/or by improving drainage therefrom and/or reducing flow rate in turbulent areas, for example by reducing flow to the areas or relaxing the vessels near the turbulence. At least as a temporary measure, the above method of flow control may be used in a trauma situation to reduce flow to hemorrhaging organs or increase flow to blood-starved organs. Such blood flow control may similarly be applied in a surgical or interventional setting, for example, to reduce bleeding.

In another exemplary embodiment of the invention, the above method of

controlling blood flow is used to selectively shunt blood between organs, even if they do not share same blood supply vessels (e.g., to within on e or two forks from the aorta). For example, reducing flow to the kidneys and GI tract so that availability of blood to the brain is increased. In some embodiments of the invention, shunting includes synchronized control of two different blood vessels.

In another exemplary embodiment of the invention, blood flow to or within an organ or body part is reduced, for example periodically or on a continuous basis, so as to cause collateral blood vessels to form and/or grow.

EXEMPLARY CONTROL BOX

Fig. 4 is a showing of an exemplary control box 400 for a flow controller in accordance with an exemplary embodiment of the invention. Control box 400 is adapted to remain outside the body. Various ones of the electrodes may be external or internal. Box 400 illustrates various controls, connectors and displays, one or more of which may be provided in accordance with exemplary embodiments of the invention.

EXEMPLARY CONTROL BOX DESIGN VARIATIONS

Box 400 is shown as adapted to attachment to the body using a strap, for example, for attachment on a leg. For such uses, a low profile box is optionally used, for example, a box having a thickness of less than 2 cm, 1cm or 5mm.

Alternatively or additionally, box 400 is provided with a pouch (not shown), e.g., for a belt or necklace, or be integrated into a watch-like device.

In an exemplary embodiment of the invention, box 400 includes exposed user controls and/or a display. Alternatively, a cover may be provided. Alternatively or additionally, a separate detachable control unit is provided. Exemplary controls include an on/off switch, a switch for selecting between night and day logic, a switch for selecting which electrodes to activate and/or sensors to read and/or a switch for selecting wave parameters, sequences and/or programs.

Optionally, box 400 includes a connector for connecting to a personal computer port, a telephone jack or a cellular telephone port, for example, for remote reporting, programming and/or analysis.

In some embodiments of the invention, an external box 400 is used with implantable electrodes. In one example, the box is used at a hospital for short-term electrification of implanted electrodes. Such electrodes may be, for example, implanted in

flesh, in a blood vessel or in another hollow conduit. Some electrodes may be implanted while others are external.

Alternatively, also control box 400 is implantable and/or integrated with an implanted device, for example a pacemaker.

In an exemplary embodiment of the invention, control and/or power connections between box 400 and some of the electrodes and/or sensor associated with controller 100 are wireless connections. In an exemplary embodiment, controller 100 comprises implantable wireless electrodes including a power source and an antenna for receiving electrification instructions form a transmitter associated with controller box 400 or another implantable portion of controller 100. Such an implantable wireless electrode may have a compact shape, such as a rod or a ball, with external electrically conducting areas. Alternatively or additionally, such an implantable wireless electrode includes at least one electrode lead extending from a compact shape.

In an exemplary implementation, controller 100 includes a processor, possibly programmed with a model of the vessel and/or tissue responses to various environmental or electrical stimuli. In an exemplary embodiment of the invention, the model is a state machine. Optionally, the processor includes a semi-permanent storage for programming and/or models. Optionally, the power supply is a separate module from the rest of the device, for example comprising a capacitor bank.

ELECTRODE GEOMETRY

Figs. 5A-5E show exemplary electrode designs in accordance with exemplary embodiments of the invention.

Fig. 5A shows a ring electrode 500. Such an electrode may include, for example, multiple electrically conducting points in its circumference or it may be a single electrically conductive portion. Alternatively, it may comprise two or more arc portion electrodes of opposing polarity. In some embodiments of the invention, electrode 500 is used for surrounding an ulcer with an electrode. Alternatively to a complete ring, an arc electrode shape or a coil electrode is used.

Fig. 5B shows a mesh electrode 502. In some embodiments of the invention, at least two points on the mesh can be individually controllable by controller 100. This allows the electrification of the electrode to be varied and/or calibrated even after it is placed or implanted. Optionally, the use of a mesh electrode allows the effective size of

the electrode to be varied. Alternatively or additionally, the mesh form may used to allow passage of air or medication or nutrients through the electrode.

In an exemplary embodiment of the invention, the electrode, for example, electrode 502, includes a reservoir of a molecule or a tube connecting to such a reservoir. The electrification of the mesh can then be used to output the molecule from the mesh and/or to drive the molecule into the nearby tissue. Such electrification may be in conjunction with electrical control of adjacent muscle or vascular tissue. Alternatively, the molecule may be provided as a separate pad. Alternatively, the molecule does not use electrical assistance (e.g., iontophoresis or electrophoresis). Exemplary molecules include medication and nutrients.

Fig. 5C shows a wire electrode 504. Such a wire electrode may include multiple electrically conductive areas, which may be separately controllable or it may be only singly controllable, with one or more electrically conductive areas defined thereon. In an exemplary embodiment of the invention, electrode 504 (or one of the other electrode designs) is deformable, allowing various electrode shapes to be achieved using a single base electrode. Alternatively or additionally, electrode 504 is a needle electrode, so that it can be inserted through the skin, to apply an electric field from inside the body, possibly providing acupuncture effects. Alternatively or additionally, the electrode is mounted on a catheter, for example, for relaxing, constricting or hyper-polarizing a blood vessel in which the catheter is located or one adjacent to it.

Optionally, the electrode or an attachment means used to attached the electrode to internal tissue is made of a bio-absorbable material, so that the electrode or electrode lead can be easily removed after a while.

Figs. 5D and 5E show simple point electrodes 506 and 508. Electrode 506 is a larger electrode, while electrode 508 is a smaller electrode. Point and area electrodes may also be a bi-polar electrode. One-time ECG electrode may also be suitable for use.

Exemplary electrode sizes include point electrodes of 0.5 mm^2 and area electrodes of between 1 cm^2 and 20 cm^2, depending on the application (e.g., ulcer size). Different sized electrodes may be provided for internal applications. Exemplary linear electrodes are 1, 5 or 10 cm long. Exemplary mesh electrodes include between 2 and 400 individual elements. Larger, smaller or intermediate values may apply in other embodiments of the invention.

Other means of stimulating the blood vessels may be used as well as electrodes, for example, magnetic field stimulators which are known in the art for producing electrical discharge in excitable tissue, such as nerve tissue. An exemplary magnetic stimulator is described in PCT publications WO 91/04071 and WO 96/16692, the disclosure of which is incorporated herein by reference.

SPECIFICITY AND SIZE OF CONTROLLED VESSEL

The specificity desired and/or size of the targeted blood vessel affects the size, location and/or electrification of the electrodes, in some exemplary embodiments of the invention. For example, the targeted blood vessels may comprise a plurality of capillaries or other small vessels in a treated area. Alternatively or additionally, the targeted vessels may comprise individual small or medium sized blood vessels, for example having an inner diameter of between 1 and 3 mm. Alternatively or additionally, the targeted vessels may comprise large blood vessels, such as those having a diameter of 5 mm or greater. Intermediate sized blood vessels may also be targeted. The vessels may be arteries or veins.

In some exemplary embodiments of the invention, the targeting is specific to avoid affecting other blood vessels. Alternatively, such effects may be ignored or any resulting adverse reactions corrected for or prevented, for example, by reducing the amount of stimulation.

Alternatively or additionally, the targeting is to avoid affecting nearby non-vascular tissues, for example muscle tissues. In an exemplary embodiment of the invention, the pulses used to affect blood vessels are timed to the activation of nearby tissue to prevent inadvertent activation thereof. Alternatively or additionally, sub-threshold pulses are used. Possibly, the stimulation of blood vessels is designed at least to prevent sensations of pain and/or of muscle contraction.

ELECTRIC FIELD FORM

Various forms of electric fields may be applied. Following are exemplary values and ranges for such fields. However, some variance is expected, for example, for different people, different vessels, different disease states and different electrification configurations, especially when such a field is applied from outside the body. In some cases, as described below, the exact parameters are determined by experimenting on the patient and/or vessel and/or disease state to determine which electrification parameters and

profiles are useful and/or do not have adverse effects.

Exemplary pulse shapes include triangular-, sine-, exponential-, rectangular- and spike- wave forms. Such wave forms (and/or other field parameters) may be mixed in a single pulse, for example as described below.

Exemplary pulse frequencies include DC, and frequencies between 0.01Hz-10kHz, for example, 0.1 Hz, 1 Hz, 10 Hz, 100Hz and 1000Hz. These frequencies may be the frequencies of the pulse or of sub-pulses within a pulse, for example, a 10 Hz square wave pulse composed of 200 10kHz spike-shaped sub-pulses close together.

The polarity may be fixed or it may vary during the pulse. In particular, balanced pulses, in which the total transferred charge is zero, may be used, to prevent various adverse reactions, as known in the art.

Various intensity levels may be used, depending, for example, on the reactivity of the target tissue, insulation of other tissue from the field and available power. Exemplary current levels are between 1μa and 500ma, for example, 10μa, 100μa, 1ma, 10ma and 100ma. Exemplary voltage levels are between 0.03V and 20V, for example, 0.15V, 0.7V, 2V and 10V. A particular type of pulse is a hyper-polarization pulse, which due to its intensity, polarization and/or duration, cause hyper-polarization and non-reactivity of the vessel walls. Such a pulse may be useful in preventing an ongoing stimuli (e.g., medication) from causing vessel constriction. In an exemplary embodiment of the invention, the tail end of a hyper-polarization pulse (or other pulses) shows a gradual decline, rather than an abrupt decline, to prevent inadvertent activation by the sudden change in current.

The duration of an applied pulse may vary, for example, between 10 ms and 50 seconds, for example, 100ms, 1 second and 20 seconds. Various duty cycles may be applied, for example, between 0.01 and 1, for example, 0.1, 0.5, 0.6 and 0.9.

In all of the above pulse parameters, intermediate, larger or smaller values may also be useful.

In general, the pulse parameters may vary during a pulse and/or between pulses, for example as described below.

Additional exemplary pulse waveforms and other pulse and sequence parameters are described in the following applications, which, although may relate to other body tissues, may nevertheless be useful, with or without modification, for blood vessel

applications: PCT/IL97/00012 and PCT/IL97/00243, the disclosures of which are incorporated herein by reference.

FIELD SYNCHRONIZATION

In some exemplary embodiments of the invention, the application of an electric field and/or changes in field parameters is performed relative to various timing events. The electric field may be applied immediately after the timing event or it may include delay or prediction of the event. In some cases, the overall timing is modified to match statistical (e.g., average, minimum, maximum and variance), rather than exact, properties of the event timings. An example of such event statistics are average waking times which can be approximated using a clock or determined more exactly using an accelerometer.

The timing of the events may be provided, for example, using an internal clock synchronized to the event schedule. Alternatively or additionally, an automatic input may be received from the source of the event, or controller 100 may itself create the event. Alternatively or additionally, a user may enter an indication that an event occurred or will occur. Alternatively or additionally, a sensor may be provided to detect the event. A response may also be synchronized to a plurality of different events that may or may not occur at a same time, for example timing to both a sensor feedback and a physical therapy event.

In an exemplary embodiment of the invention, the synchronization is to a local event, for example, a local constriction of blood vessels or a local arrival of a pulse wave. Alternatively or additionally, the synchronization is to a systemic event, for example, heart beat, breathing or steeping action. Alternatively or additionally, the synchronization is to a remote local even, for example, arrival of a pulse wave or a muscle contraction at a knee, when the treated area is in the foot. In some case, the remote tissue may be easier to monitor and/or such monitoring may indicate an adverse effect at the remote location.

Alternatively or additionally, the synchronization is to environmental or lifestyle events, for example, exterior temperature, ingestion of food and time of day (e.g., sleep).

Alternatively or additionally, the synchronization is to a physical therapy, for example, medication, heat therapy or electrical therapy (e.g. for pain relief or for control of body tissue other than blood vessels).

Alternatively or additionally, the synchronization is to an organ output or activity cycle, for example, the location of a peristalsis wave in the GI tract and/or the rate of

generation of acid in the stomach.

ELECTRIFICATION PROFILES

When applying the pulse, the electrical properties may be uncontrolled. In an exemplary embodiment of the invention, however, the electrical properties are controlled, for example, the voltage, current, power and/or total charge.

In some exemplary embodiments of the invention, the pulses are applied as trains, for example, including a pacing pulse and a controlling pulse, with the pacing pulse causing contraction and the controlling pulse modifying properties of the contraction, such as its duration or intensity. Alternatively or additionally, trains may be applied for other reasons, for example, to assure capture or to provide a greater total charge than possible with a single pulse.

Figs. 6A-6B show exemplary electrification wave forms in accordance with exemplary embodiments of the invention;

Fig. 6A shows a train of alternating hi-frequency and low frequency pulse sections, which may be used in some embodiments of the invention. In the example shown, also the pulse intensity varies.

Fig. 6B shows a train of random duration balanced pulses, which may be used in some embodiments of the invention.

Another parameter that may be used to define the applied field is the pulse envelope. For example, the applied intensity may be increased over the time of a single train, to compensate for an expected increase in tissue resistance (or vice-versa), or to ensure capture of less sensitive tissues.

Depending on the effect to be achieved, the application of a single train may not be sufficient. In some embodiments of the invention a long train of pulses is applied, for example, 5, 10, 500, 1000 or even 5000 seconds long, or any intermediate, larger or smaller durations. Alternatively or additionally, a sequence of pulses or pulse trains is applied, possibly with relatively long delays between the trains, for example, delays of 10, 100 or 1000 seconds. For some disorders or preventive situations, pulses may be applied over a long period, for example a few hours or a few days or weeks. For example, preventing pooling of blood or increasing blood flow to an area that has diminished blood flow may include multiple daily sessions applied over a long period of time (e.g. 10 minutes, 10 times a day, for one month or forever). Exemplary pulse/train repetition rates

include 1/sec, 1/minute, 1/hour, 1/day and/or any intermediate or greater or smaller rate.

In some applications, the applied pulses and/or pulse application rate may change over time, for example as therapy progresses, as electrodes become less conductive and/or to compensate for conditioning of the body. Alternatively or additionally, an associated therapy may be varied to compensate for such long term changes. Alternatively or additionally, steroids may be provided at the electrodes, to prevent their efficiency from degrading.

In some applications an additional electrical therapy is provided. While this therapy may use other electrodes or be applied at other times than vessel control therapy, in some embodiments of the invention, a combined pulse having both vessel effects and non-vessel effect is used. Optionally, the more sensitive tissue is targeted by the first portion of the pulse. Alternatively or additionally, both tissues are targeted by a same portion of the pulse.

In some applications, different tissues portions are selected (e.g., based on electrode location) for control at different times, for example, different axial and/or radial sections of a blood vessel. In an exemplary embodiment of the invention, this selection is directed at preventing over stimulation of a same section, which can possibly cause conditioning or exhaustion of the vessel. Alternatively or additionally, the alternation is to provide exercising of the vessel. Alternatively or additionally, such alternation is used to vary the treatment, for example, how pooled blood is returned or which part of an ulcer gets an increased blood flow. Such alternation may also be useful when the total supply of blood is limited and a suitable increased flow cannot be supplied to all parts of the treated tissue at a same time.

EXEMPLARY VARYING PULSE SCHEDULES

Following are some exemplary situations where the pulse application will be varied. Suitable sensors and additional therapies will be described below.

In one exemplary embodiment of treating an ulcer in an extremity, a sensor is provided along the venous return to detect pooling of blood caused by an increase in flow greater that the venous return capability. Such pooling may also be a separately treated condition. Possibly, such pooling initiates a sequence of striated or vascular muscle contraction to assist venous pumping. Alternatively or additionally, an alert is generated to the patient. Alternatively or additionally, the degree and/or repetition rate of the blood

flow increasing therapy is reduced. Alternatively or additionally, a blood flow reducing therapy is applied.

In an exemplary embodiment of treating Raynaud's disease or phenomenon, blood flow to the fingers is increased in response to a low sensed environmental temperature, low extremity temperature and/or detection of reduced flow volume. Such an increase in flow may shunt blood flow away from other parts of the extremity, especially in a patient where normal flow compensation and/or feedback mechanisms are damaged. A sensor is possibly provided over an area which is determined (e.g., based on a model or experimentation) to be susceptible to such reduced flow. When reduced flow is detected, the Raynaud specific therapy may be stopped, reduced or reversed and/or similar therapy applied to the susceptible area or to an artery further upstream.

In another exemplary embodiment of the invention, the electric field is synchronized to a physical therapy application. For example, the electric field is applied before, during and/or after a heating therapy, such as ultrasound or microwave radiation. Optionally, vessel relaxation is applied during or after the heating, to prevent hyperthermia. Alternatively or additionally, vessel constriction is applied before or during the heat wave, to prevent heat dissipation. In another application, blood flow is increased in conjunction with therapeutic muscle activation.

In another exemplary embodiment, the field application is synchronized to an arrival of a pressure pulse wave, so as to most efficiently increase or reduce perfusion by selective relaxation/constriction.

Alternatively or additionally, to including circuitry for applying such various pulse schedules, in an exemplary embodiment of the invention, controller 100 includes one or more watchdogs, for ensuring safety. Such watchdogs may automatically stop or cut off an existing therapy, generate an alert and/or apply a counter-therapy, for example if the therapy is not working, overly high fields are applied and/or adverse effects are detected.. In an exemplary embodiment of the invention, the watchdog logic is separate from the main logic.

ELECTRODE LOCATION AND ORIENTATION

Referring back to Fig. 1, the electrodes (and sensors) may be located at various locations relative to a treated tissue. In one example, remote electrodes such as electrodes 150 and 152 are provided to apply fields to areas remote from the treatment area, for

example, to prevent venous blood pooling and/or affect an upstream supply vessel.

In a nutrient flow modulation example, electrodes are placed on ulcer 110 itself. In an example of increasing flow to ulcer 110, electrodes are placed near the ulcer, to relax adjacent capillaries and other small vessels.

In an exemplary embodiment of the invention, electrodes of opposite polarity are placed near the area to be treated and/or affected. Alternatively or additionally, one electrode, for example with positive, negative or changing polarity is placed locally and another electrode is placed at a remote location, for current flow reasons.

In some exemplary embodiments of the invention, programmable electrodes are provided, for example linear (possibly deformable) or mesh electrodes. Controller 100 may selectively electrify different ones of the electrodes in order to achieve a desired field. In some cases, the electrification of the electrode is changed during a pulse train or sequence, to achieve various effects, for example, tissue selection or molecule transport. Optionally, control box 120 serves as one of the electrodes. Alternatively, box 120 may comprise at least two electrodes, for example, if box 120 is placed directed on an area to be treated and/or a blood vessel to be affected.

Electrode orientation can be varied as well. Two possible reasons for selecting a particular electrode orientation are more accurately selecting which blood vessel of several nearby vessels (or other tissue) to affect and selectively controlling a particular one of the multiple muscle layers in a vessel. It is hypothesized that at least for some vessels the smooth muscle fibers of the vessel exhibit a directional sensitivity variation, which may be used for such selectivity. Alternatively or additionally, an electrode may be provided into the blood vessel wall, near the muscle layer which is to be affected. Alternatively or additionally, a differential activation effect is achieved by activating more extensive radial extents than axial extents, for example, by applying a field to complete, thin, rings around a blood vessel, so that the total axial effect is made small. Alternatively or additionally, smaller vessels only have one layer of musculature.

US patent 6,041,252, the disclosure of which is incorporated herein by reference describes various electrode configurations that allow an electric field to be effectively contained within a desired volume. Such an electrode placement and electrification scheme may also be used to assist selectivity and/or prevent unnecessary interactions with nearby tissue.

ELECTRODE OUTFITTING

In an exemplary embodiment of the invention, a general purpose controller 100 is provided, for example, as a small or large control box 120 with ports for attaching various electrodes. Such a device may be programmed to the particular therapy desired.

Alternatively, a dedicated device and/or electrode design is used.

Figs. 7A-7C show exemplary electrode halter arrangements in accordance with exemplary embodiments of the invention. In general, the halter (if any) may be integrated with a garment, for example, the electrodes being removable or non-removable from the garment. Alternatively, the garment may include an indication of where to attach the electrodes. Alternatively or additionally, the garment may support the control box for the electrodes.

Optionally, the garment and/or the electrodes are one time use, which are disposed after use.

Fig. 7A illustrates a pair of therapeutic shorts 700, including a halter 702, for use in erectile dysfunction. In this application, it may be desirable to have the halter separable from the shorts so that the shorts can be selectively removed. A similar application using a tampon may be used for female sexual dysfunction.

In the embodiment shown, halter 702 optionally includes one or more controls 704 and an attachment to blood flow increasing electrodes 706. In some embodiments, the electrodes may be placed on the penis, with multiple electrodes optionally being provided to allow various protocols of relaxation/contraction of blood vessels leading to and in the penis. Optional electrodes 708 for stimulating abductor muscles may also be provide don halter 702. An exemplary arc-shaped sensor 710 is shown, for detecting an effect on penile stiffness and/or diameter as a result of the electric field application. Other sensor types and/or sensor locations may be used. Optionally, halter 702 can also be used to selectively relax penile blood vessels, to as to prevent overly long erections. A built in timer watchdog may be provided for this function.

Fig. 7B illustrates a glove-halter 720, which utilizes heating elements 724 in addition to blood-flow affecting electrodes 722. In an exemplary embodiment of the invention, electrodes 722 are bipolar electrodes. Alternatively, electrodes 722 may share a remote common electrode, for example in a control box 726. Alternatively, control box 26 may be remote from the glove, for example in a wrist or waist band.

Fig. 7C illustrates a glasses-based flow control device 730, in which electrodes 732 and optional additional electrodes or sensors 734 are integrated into glasses 736. Optionally, the control box functionality is also integrated into glasses 736.

Other exemplary implementations include a bracelet or arm band with integral or wire-extending electrodes, a sock or leg band implementation and a wing device including integral electrodes and optionally sensors for electrifying scalp blood vessels.

SENSOR PROPERTIES

Various types of sensors may be used with controller 100. Different sensors may be desirable for different applications and/or for general purpose devices.

Substantially independently of the sensor modality, a sensor may be wireless or connected to controller 100 by a wire. Some sensors may be integrated into control box 120, for example a pulse wave sensor or an ambient temperature sensor.

A sensor may be always attached. Alternatively, a patient may periodically attach or activate the sensor. Some types of automated sensors may also be activated only periodically, for example, to conserve power and/or other limited availability, such as a chemical reagent in the sensor. Even continuously operated sensors may be read continuously or periodically, for example, depending on the logic used to operate controller 100.

Some sensors are non-invasive, for example surface electrodes. Other sensors are invasive, for example being mounted on pins that penetrate the skin and/or may require invasive operations, for example letting of blood, to provide readings. Other sensors may be totally implanted

Although for many applications the sensors do not require operator assistance, some types of sensors require some amount of patient (or caretaker) intervention, for example, dip-stick sensors for glucose in urine or blood and dip stick detector for pathogens and chemicals.

In an exemplary embodiment of the invention, sensors that are integrated with the electrodes are used. Such sensors may be electrically-sensitive sensors, for example impedance sensors, or simply sensors whose structure allows them to be provided in integrated form with one or more electrodes.

EXEMPLARY SENSORS

Many physiological sensors and sensor types are known in the art and most if not

all can find use in one application or another in accordance with exemplary embodiments of the invention. However, the following is a list of some exemplary sensors which may be useful:

(a) Blood characteristics sensors, such as impedance sensors (for volume or flow), flow sensors, oxygenation sensors, Doppler sensors and pressure sensors (for detecting pulse wave).

(b) Temperature sensors;

(c) chemical sensors, for example, pH, hormones, perspiration components, extrudes of ulcer and glucose;

(d) biological sensors, for example for detecting pathogens, some of which sensors may require preparation of the biological sample (e.g., feces) by a patient, caregiver or operator;

(e) skin and ambient humidity sensors;

(f) breathing cup for detecting materials, for example ketone levels in breath and/or for measuring inhalation/exhalation rate and/or volume;

(g) vessel shape sensors, for example imaging or non-imaging ultrasound, to detect the size, shape and/or changes in geometry of a vessel in response to the application of a field, force transducers to detect tensions and/or accelerometers to detect motion (due to contraction/relaxation);

(h) electrical sensors, for example, for EMG or ECG; and/or

(i) saliva pH sensors (possibly manually applied).

EXEMPLARY USAGE

Fig. 8A is a flowchart 800 of an exemplary process of using a controller 100, in accordance with an exemplary embodiment of the invention.

At 802, a patient is diagnosed with a disease state and/or a pre-clinical state (e.g., diabetes and low blood flow to the feet), for which controller 100 can apply preventive and/or therapeutic treatment. In some cases, the diagnosis and/or determination that controller 100 may be suitable is achieved by the patient wearing controller 100 at least for data collection purposes and optionally, for the effects of testing various pulse sequences.

At 804, the patient is fitted with controller 100, for example a general purpose controller or a disease-specific controller.

At 806, the controller is calibrated, for example, to apply suitable pulses and/or

detect various adverse reactions. More details are provided with Fig. 8B below. Optionally, at least some of the calibration process is performed before the patient is fitted. However, with external electrodes, it may be preferable to calibrate once the controller is in place.

While the controller is in use, a patient may control various aspects of its operation (808). For example, a patient may be required to assist in data collection (e.g., dip stick and blood chemistry sensors). Alternatively or additionally, a patient may enter an indication of an event, for example, a meal (e.g., so a higher blood nutrient level is expected), an upcoming sleep period or exercise level (e.g. sitting at a desk). Alternatively or additionally, a patient may change the device function, for example by selecting between treatment programs and/or setting a treatment intensity (e.g., in case of a migraine). Optionally, controller 100 compensates for patient input, for example, by providing a gradual increase in activity and/or applying watchdog functions to prevent over-treatment. Alternatively or additionally, controller 100 provides patient alerts (e.g., failed treatment, adverse reaction or device malfunction).

Optionally, controller 100 include reminder and querying functions, for example to remind a patient to perform exercise or report on his state, for example as described in PCT publication WO00/47108, the disclosure of which is incorporated herein by reference.

At 810, long-term check-ups are performed, for example, via remote communication or by the patient coming into a clinic. Optionally, as a result of such a check-up the device parameters may be changed and/or the patient may be re-diagnosed. These check-ups may be periodic and/or programmed into controller 100.

CALIBRATION

Fig. 8B is a flowchart 820 of a method of calibrating a controller 100 in accordance with an exemplary embodiment of the invention.

At 822, the target controller or a programmable (e.g., bedside) controller is attached to the patient.

At 824, one or more test pulses, trains and/or sequences are applied to the patient. Various sensor and electrode configurations may also be tested. At 826, positive effects of the pulses are detected. At 828, negative effects of the pulses (e.g., pain or blood pooling) are detected.

Steps 824-828 may be repeated several times, for example, to cover a range of possible pulse parameters.

At 830, the results of the testing are analyzed to select a treatment protocol, which determines the programming and/or parameter settings for controller 100.

Alternatively, or as a starting point for applying test sequences (824) a database of pulse parameter values and their effects on other patients may be used to select the programming.

Some programming information may be manually entered in any case, for example, the diagnosis and expected schedule of periodic therapy, such as insulin injection.

Once the controller is programmed and in use, the actually applied pulses and their effects may be logged (832) optionally, a plurality of test pulses may also be applied, automatically or manually, to determine their effect. During a long term check-up, the programming may be reconfigured (836) to take into account the logged data. Such reconfiguring may be manual or it may be automatic.

Some programmable values may be automatically determined. One example is perfusion level. In a patient having an organ with healthy and diseased parts, a reading at the healthy part may be used to automatically determine a desired level in the diseased part (e.g., blood flow). Alternatively or additionally, even if a function relating a physiological parameter to a controlled variable is programmed, the actual degree of control may depend on a measurement, for example, blood flow to kidney may be dependent on an actual urine concentration.

EXEMPLARY PROGRAMMABLE PARAMETERS

Although substantially any of the above described features and parameters may be programmable, following is an exemplary list of types of parameters, one or more of which may be programmable in some embodiments of controller 100.

(a) pulse, pulse train and/or pulse sequence parameters;

(b) electrification order and/or selection of electrodes or electrode components;

(c) thresholds of applied fields;

(d) parameters of an additional therapy applied or coordinated by controller 100;

(e) selection of sensors to use;

(f) relationship between sensed variables and treatment to effect;

(g) adverse effect sensor threshold levels;

(h) response to adverse and/or positive effect detection

(i) device logic, for example time dependency, long term dependency; and/or

(j) range of user inputs to accept.

EXEMPLARY APPLICATIONS AND EFFECTS

Although a multiplicity of various therapies and disease states are described above, below is an additional listing of various therapeutic effects that may be achieved using a suitably programmed controller 100.

ULCERS, GI, DIABETES AND PRESSURE SORES

Increase in blood flow may assist in healing or prevention of ulcer. Alternatively or additionally, iontophoresis is used to ensure nutrients cross tissue between blood vessels (or artificial nutrient source) and tissue near ulcer. In GI ulcer, activity of GI tract may be modulated as well, using electrical control of the GI muscles.

In case of pressure sores, increase in flow may be timed to when a patient is moved to a different position. Such motion may be detected using an accelerometer.

Optionally, striated muscles are contracted to assist venous return from ulcerated organ.

A potential advantage of electrical therapy for ulcers is that electric fields can penetrate deeper than topical creams, possibly without associated systemic problems.

A potential problem with some ulcers is providing suitable penetration of the electric field past the ulcer. In some embodiments of the invention, a conducting cream is used to couple the electrode to the ulcer. Alternatively or additionally, an increased intensity electric field is used.

In an exemplary embodiment of the invention, ulcers are prevented by maintaining relaxed near-surface blood vessels, to ensure perfusion. Alternatively or additionally, in pressure sores, near surface blood vessels are relaxed to compensate for damaged blood vessels.

In an exemplary embodiment of the invention, a pressure-sore treatment mattress or mattress pad is provided. Such a mattress provides electrical fields for relaxing and/or contracting near-surface blood vessels. Optionally, such fields are activated only at areas adjacent high pressure areas, detected, for example using an array of pressure sensors.

In an exemplary embodiment of the invention, the electric field intensities are

cycled between high and low values. Such cycling may ensure capture. Alternatively or additionally, such cycling may provide both relaxation and contraction of blood vessels, possibly preventing or reversing pressure damage to the vessels. In an exemplary embodiment of the invention, a Doppler ultrasound or laser perfusion meter is used, possibly through the bedding to determine an effect of the electric fields.

It should be noted that diabetes and certain motion-restricting illnesses are often associated with decreased nervous sensation so that some excitation (intentional and/or inadvertent) of striated muscles, may be below a patient's threshold.

An exemplary sensor is a wetness sensor for detecting wetness at the ulcer caused by the increased flow. Such wetness may also indicate that local medication is being carried away, so an increased dosage is desirable (possibly applied by controller 100).

STENT

Where a stent is installed to widen a conduit in the body, for example in a blood vessel or a body conduit, electrification of the stent may be used to relax surrounding vascular (and/or other) tissue. Such relaxation may be continuous or it may be cyclic, for example, to assist in restoring normal vascular muscle tone. Alternatively or additionally, the relaxation may apply to nearby vessel portions, in which no stent was installed, but which may also suffer from stenosis. Alternatively or additionally, the motion or prevention of motion of the vessel wall may prevent re-stenosis.

An exemplary sensor is a stenosis degree sensor or a flow volume or rate sensor.

INFLAMMATION

Increased blood flow may be useful, for example, to prevent a generalized inflammation response, by washing away inflammation causing signaling chemicals. Alternatively or additionally, intelligent blood flow increase may be more effective in actually increasing blood flow than the general flow increase caused by body mechanisms, especially in a diseased patient.

Blood drainage (and an associated blood pooling sensor) may be monitored and/or managed.

Such increased blood flow may also be useful for draining pus and washing away pathogens or toxins created by them. In some case, reduced blood flow is desired, to prevent dissemination of toxins and/or washing away of locally applied medication.

Drainage of blisters and swellings is also achieved in some embodiments of the

invention.

In some cases, the blood flow is cycled between high and low, for example, in order to overcome automatic body compensation mechanisms or in order to activate such mechanism.

SPORE SETTLEMENT PREVENTION

Some types of diseases such as trypsanomyasis (sleeping sickness) and trichinosis may possibly be regulated by reducing flow to susceptible organs selectively diverting flow within the organ to less important portions thereof and/or increasing flow, so as to wash the spores away. In the case of trichinosis, simultaneous muscle activation may be desirable.

GLANDULAR OUTPUT CONTROL

In an exemplary embodiment of the invention, blood flow to a pancreas or another gland, such as an adrenal gland is reduced, so as to reduce its metabolic activity and output. Alternatively, such a reduction may be used to maintain the gland's activity, for example, reducing blood flow to an adrenal gland when a bolus of steroids is provided, so that the adrenal gland does not sense extremely high levels of steroids and shut off. Alternatively, such reduced blood flow increases the local concentrations of glandular output, thereby activating production feedback mechanisms.

If other means of controlling hormone output are provided (e.g., medication or electrical control), blood flow may be increased when such means is applied, to further selectively produce one hormone over other hormones in the gland.

An exemplary sensor for feedback is a hormone level sensor.

TOXIN REMOVAL

Increased flow in the liver, can assist in removing toxins from the blood. Conversely, reduced flow through diseased parts off the liver may reduce the advance of cirrhosis in such semi-damaged portions. Alternatively or additionally, increased flow may be used in the pancreas or other organs to wash away toxins.

An exemplary sensor for feedback is a blood flow sensor for sensing relative blood flow in different parts of the liver.

STONE TREATMENT

Prevention of flow to a part of the kidney or gall bladder where a stone is forming may prevent further growth and/or assist in its dissolution. Alternatively or additionally,

flow may be increased, particularly when a stone-dissolving treatment, such as medication is applied. Alternatively or additionally, flow may be reduced, when stone forming chemicals are in a high blood concentration. Increased or reduced flow may also be used to modify the blood pressure sensed by the kidney, thus possibly indirectly modifying the body blood pressure and/or to modify the osmotic pressure in the kidney, thus possibly affecting urine components concentration.

A suitable exemplary sensor is an ultrasound reflection sensor, that senses a stone size based on the amplitude of reflection therefrom.

PERFUSION ENHANCEMENT

In addition to ulcers, mentioned above, increased blood flow (possibly measured using an oxygenation sensor) may be used to treat tissues infected with anaerobic bacteria, such as clostridia perfinges, tetanus or gas gangrene. Muscle activation (e.g., electrical stimulation or exercise) may also assist blood flow.

DIALYSIS

In an exemplary embodiment of the invention, constriction of a vein is used to increase the pressure in a vein, instead of performing a shunt between the venous and arterial systems. Alternatively, a shunt in smaller blood vessels may be sufficient.

In an exemplary embodiment of the invention, the constriction of the vein is constant. Optionally, electrical activation of the striated muscles is provided as well, to increase venous pumping action and increase venous pressure. Such pumping action may also be used in conjunction with other methods of constricting the vein.

Alternatively or additionally, the vein may be cycled between contraction and relaxation, to effect a pumping action.

Possibly, long term cycling of a vein will cause the vein to develop additional muscular tissue. Optionally, such a muscular vein is developed in anticipation of a bypass procedure, in which the vein will be used in place of an artery.

PAIN CONTROL

Some types of pain, for example angina pectoris, are caused by blood flow restrictions. Migraine headaches and tensions headaches are also believed to have such causes. In an exemplary embodiment of the invention, electrical control is used to relax such muscles. An exemplary sensor is a flow volume or vessel diameter sensors (e.g., ultrasound).

In an exemplary embodiment of the invention, the electrical control is assisted by scalp massage (using electrical stimulation of scalp muscles)

PSYCHIATRIC EFFECTS

It may be possible to modulate some types of psychiatric illnesses by modifying blood flow to the brain and/or within the brain. For example, increased (or reduced) flow within the brain may assist in reducing (or increasing) local concentrations of neurotransmitters. Exemplary diseases include schizophrenia and ADHD. Optionally, such a treatment is associated with stimulation of hormone producing glands, such as those producing Seratonin, Epinephrine and Nor Epinephrine.

Exemplary sensors include a blood flow sensor, a perfusion sensor and a hormone/neurotransmitter sensor. However, user or caretaker input and/or notes from other patients may be especially useful in psychiatric applications.

FAT CELLS DIMINISHMENT

Modulation of blood flow to fat cells may yield short term and/or long term effects. As a long term effect, necrosis of the cells or reduced flow to the cells may be achieved. As a short term effect, metabolizing of fat in the cells and/or prevention of depositing of new fat may be achieved. Modulation of flow may be combined with local or remote stimulation of muscles, so that muscles utilize energy.

Optionally, the electrical control is timed to activities such as meals and exercise and/or to blood levels of glucose, insulin and/or fatty acids.

Optionally, by selectively redirecting flow between different body parts, redistribution of fat is achieved.

Exemplary feedback sensors include sensors for metabolic products of fat and fat cells and blood flow sensors.

NECROSIS PROMOTION

In an exemplary embodiment of the invention, blood flow to a tumor is reduced and/or cycled, possibly in conjunction with the application of a cancer-fighting agent and/or hyperthermia. Reduced flow can assist in increasing local concentrations of materials toxin to the tumor, prevent heat dissipation and/or starve the tumor.

GI TRACT

Increasing or reducing blood flow to the GI tract may increase or reduce its activity and/or increase or reduce nutrient absorption. Alternatively or additionally, decreased

blood flow prevents or inhibits some types of diarrhea. In some embodiments, promotion of diarrhea is provided by blood flow modification.

Optionally, control of blood flow is applied in conjunction with electrical control of the peristalsis. As in other combined therapies, in addition to generally parallel activity, the vascular effect may assist the other therapy, prevent adverse effects therefrom, interact in a synergistic manner therewith and/or the other therapy may be provided to prevent or treat adverse effects caused by the vascular therapy.

Exemplary sensors includes, pressure sensor (for strength of GI tract contractions) and blood flow sensors.

ORGAN IMPLANT

An implanted organ may suffer from decreased blood flow. In an exemplary embodiment of the invention, an abnormally increased blood flow is provided to prevent rejection. Alternatively or additionally, a reduced blood flow is provided, especially when the blood is loaded with substrate for the organ (e.g. a kidney or liver) , for example, to reduce the workload on the organ.

Exemplary sensors include blood level chemical sensors and organ output sensors (e.g., urine volume sensor).

EXPERIMENTAL RESULTS

Reference is now made to Figs. 9A, 10A, 11A, 12A and 13A which graphically show the effects of electric fields applied to an isolated section of the ascending aorta 920 of a rabbit, during a series of experiments performed in accordance with various embodiments of the present invention.

Fig. 9B shows the setup of an isolated aortic section 920 that is bathed in a physiologic solution 914. A DC electric field 900 is applied through two identical electrodes 910 and 912 placed adjacent to artery 920. In Fig. 9A the electric field 900 is increased at 40 seconds to 15 mA (906) for approximately 10 seconds and then removed (904). The aorta was prepared by cutting a ring out of the aorta. In some experiments, the ring was cut. One side of the ring (or cut ring) was attached to a base and the other side of the ring was attached to a second base, via a strain gauge.

Graph 924 demonstrates muscle tension of aorta 920. During the period when no current is applied, muscle tension 922 of aorta 920 shows a mild decrease in tension. When the 15 mA current is applied (906), muscle tension of aorta 920 increases along a

graph section 902, from approximately 1.15 grams of tension to 1.32 grams of tension. When the current is removed, muscle tension of aorta 920 drops (926) and continues to revert to its original tension level (924). This experiment demonstrates that tension of aorta 920 increases rapidly as a result of the application of an electric field and decreases with removal of the electric field.

Since blood flow is reduced when muscle tension increases, this experiment demonstrates that an electric field is an effective means of reducing blood flow in an artery.

Fig. 10B shows a setup similar to that of Fig. 9B, except that two unequally sized electrodes 1010 and 1012 are used instead of equal sized electrodes for applying an electric field to an aortic section 1020 bathed in a physiologic solution 1014. Electrode 1010 is larger than electrode 1012. Graph 1000 shows the application of an electric field 1006, of about 8mA (1006) which is maintained for approximately 130 seconds and then removed (1004). Graph 1002 shows the response of the aorta to the field. During the application of electric field 1022, aortic tension decreases from approximately .95 grams of tension to about .65 grams of tension. When the electric field is removed, muscle tension increases gradually to .90 grams of tension (1026).

This experiment demonstrates that an electric field applied to an aorta via unevenly sized electrodes can reduce the tension of muscles of aorta. Since reduced muscle tension allows blood flow to increase, this demonstrates that an electric field is an effective means of increasing flow in an artery.

Fig. 11B shows a setup similar to that of Fig. 10B, with two unequally sized electrodes 1110 and 1112. Potassium Chloride 1132, an agent that increases artery muscle tension, is added to physiologic solution 1114. During the period when there is no electric field 1100, tension (1126) of aorta 1120 gradually increases due to the effect of Potassium Chloride. When an 8 mA electric field is applied (1106), the aortic tension (1122) stops increasing. When the electric field is removed (1104), the aortic tension again increases (1128). Finally, when the electric field of 8mA is applied again (1134), the aortic tension (1130) again stops its increase.

This experiment demonstrates that an electric field can stop the aortic tension increase due to the effect of Potassium Chloride. Since aortic constriction decreases blood flow, this shows that an electric field can prevent the effects of a stimulus that restricts

blood flow. An analogous situation occurs in Raynaud's disease or phenomenon, where environmental cold causes a severe increases in artery muscle tension, causing a painful restriction of blood flow. Such an electric field could prevent the decreased blood flow due to Raynaud's disease or phenomenon from taking effect.

Fig. 12B shows a setup similar to that of Fig. 10B, with a direct current being applied to aortic section 1220 through two unequally sized electrodes 1210 and 1212 in physiologic solution. Here, two connections 1240 and 1242 are in place in order to deliver a current of opposite the polarity through electrodes 1210 and 1212.

During the period when a negative current 1206 is applied, the tension in aorta 1220 increases (1222) to approximately 1.5 grams. When the current is removed, (1204) the tension of aorta 1220 decreases gradually (1228). As a positive electric current 1234 is applied, the decrease in aortic tension (1226) is more rapid. Finally, when the current is removed (1236), aortic tension (1242) remains constant at approximately its original level.

This experiment demonstrates that an electric field can increase aortic tension and that an electric field of opposite polarity can decrease aortic tension. Since aortic tension constricts the aorta and impedes blood flow, and aortic relaxation increases blood flow, this demonstrates that an electric field can both decrease and increase blood flow. These effects may also be related to the sizes of the electrodes, the distance between them and/or the associated charge densities.

Fig. 13B shows a setup similar to that of Fig. 10B, with two unequally sized electrodes 1310 and 1312 that deliver a DC electric field to an aorta 1320. In addition, two equal sized electrodes 1340 and 1342 are applied to the aorta for delivering an AC electric field.

In a graph 1300, we see an electric field of approximately 8mA (1306) being applied. This causes a decrease in aortic tension (1322). When the electric field is stopped, (1304), the aortic tension increases (1350). Upon resumption of the electric field (1334) the aortic tension again decreases (1336). With the removal of the electric current (1364) the aortic tension increases slightly (1326). Now, referring to a graph 1360, that records the AC electric field applied through electrodes 1340 and 1342, a DC offset, rapidly alternating electric field 1354 is applied (shown as a shaded rectangle). The aortic tension 1356 is seen to increase rapidly. When the alternating electric field is removed, the aortic tension decreases (1362).

Electric field 1300 shows that an aorta responds to two increases in direct current with a brief rest in-between and demonstrates that habituation of response in blood flow can be avoided, at least in some situations.

AC Electric field 1360 shows that the return of the aortic tension to its original tension (1362), can be greatly speeded by the application of alternating current pulse 1354. This effect is important in utilizing a feedback system. When the feedback senses the need for a rapid change in blood flow, it need not rely on stopping the electric field so that the blood vessel responds gradually. Instead, the feedback mechanism can apply an alternative type of electric field, such as an AC electric field, and rapidly effect such a change.

It will be appreciated that the above-described methods of electrifying vascular and/or non-vascular tissues may be varied in many ways. In addition, a multiplicity of various features, both of methods and of devices has been described. Where methods are described, devices for carrying out the methods are also contemplated. It should be appreciated that different features may be combined in different ways. In particular, not all the features shown above in a particular embodiment are necessary in every similar exemplary embodiment of the invention. Further, combinations of the above features from different exemplary embodiments are also considered to be within the scope of some exemplary embodiments of the invention. Also within the scope of the invention are devices and/or software for programming existing devices to make the device comply with the methods described herein. Section headings where they appear are meant for clarity of browsing only and should not be construed as limiting the contents of a section to that particular section. When used in the following claims, the terms "comprises", "includes", "have " and their conjugates mean "including but not limited to".

It will be appreciated by a person skilled in the art that the present invention is not limited by what has thus far been described. Rather, the scope of the present invention is limited only by the following claims.

CLAIMS

1. A method of treating tissue with a problem of reduced nutrient availability, comprising:

selecting at least one blood vessel associated with a peripheral body tissue having a reduced nutrient availability;

selecting a location adjacent said selected blood vessel; and

electrifying said selected blood vessel from said location with an electric field that modifies blood flow associated with said tissue by directly acting on said blood vessel,

wherein said tissue comprises peripheral body tissue.

2. A method according to claim 1, wherein said blood vessel comprises an artery.

3. A method according to claim 1, wherein said blood vessel comprises a vein.

4. A method according to claim 1, wherein said blood vessel comprises a capillary bed.

5. A method according to claim 1, wherein said location is on said treated tissue.

6. A method according to claim 1, wherein said location is adjacent said treated tissue.

7. A method according to claim 1, wherein said location is remote from said treated tissue.

8. A method according to claim 1, wherein said electrification increases blood flow to said treated tissue.

9. A method according to claim 1, wherein said electrification increases drainage from said tissue.

10. A method according to any of claims 1-9, wherein said electrification is timed relative to a motion of an organ associated with said treated tissue.

11. A method according to claim 10, wherein said organ comprises an appendage.

12. A method according to any of claims 1-9, wherein said electrification is timed relative to an arrival of a pulse wave at the treated tissue or the location.

13. A method according to any of claims 1-9, comprising periodically repeating said electrification.

14. A method according to claim 13, wherein said repeated electrifications are the same.

15. A method according to claim 13, wherein said repeated electrifications have at least one changed parameter.

16. A method according to any of claims 1-9, wherein said selecting comprises selecting a vessel associated with ulcerous tissue.

17. A method according to any of claims 1-9, wherein said selecting comprises selecting a vessel associated with pre-ulcerous tissue.

18. A method according to any of claims 1-9, comprising locally providing a molecule to said ulcer.

19. A method according to claim 18, wherein said provision is assisted by said electrification.

20. A method according to claim 1, wherein selecting comprises selecting a single blood vessel.

21. A method according to claim 1, wherein selecting comprises selecting multiple blood vessels.

22. A method according to any of claims 1-9, comprising:
receiving an indication of an ambient environmental condition; and
applying said electrification responsive to said indication.

23. A method according to any of claims 1-9, comprising:
receiving an indication of an effect of said electrification; and
varying said electrification responsive to said indication.

24. A method according to claim 23, wherein said effect comprises a change in blood flow.

25. A method according to claim 23, wherein said effect comprises a therapeutic effect of said electrification.

26. A method according to claim 23, wherein said effect comprises an adverse effect of said electrification.

27. A method according to any of claims 1-9, wherein said treated tissue comprises diabetes-mellitus affected tissue.

28. A method according to any of claims 1-9, wherein said treated tissue comprises Raynaurd's-disease affected tissue.

29. A method according to any of claims 1-9, wherein said treated tissue comprises pressure sore tissue.

30. A method according to claim 23, wherein said varying reduces an effect of said field.

31. A method according to claim 23, wherein said varying stops an effect of said field.

32. A method according to claim 23, wherein said varying reverses an effect of said field.

33. A method of treating a tissue condition, comprising:

electrifying a selected blood vessel with an electric field that modifies blood flow associated with a treated tissue by directly acting on said blood vessel,

receiving an automatic indication of a local effect of said electrification; and

varying said electrification responsive to said indication.

34. A method according to claim 33, wherein said effect comprises a change in blood flow.

35. A method according to claim 34, wherein said effect comprises an increase in blood flow.

36. A method according to claim 33, wherein said effect comprises a therapeutic effect of said electrification.

37. A method according to claim 36, wherein said therapeutic effect comprises an increase in an activity of said tissue.

38. A method according to claim 36, wherein said therapeutic effect comprises a reduction in an activity of said tissue.

39. A method according to claim 36, wherein said therapeutic effect comprises a modification of a molecule level in said tissue.

40. A method according to claim 39, wherein said molecule comprises a nutrient.

41. A method according to claim 39, wherein said molecule comprises a medication level in said tissue.

42. A method according to claim 39, wherein said molecule comprises a toxic molecule.

43. A method according to claim 39, wherein said molecule comprises a hormone.

44. A method according to claim 39, wherein said modification comprises an increase in the molecule level.

45. A method according to claim 39, wherein said modification comprises a decrease in the molecule level.

46. A method according to claim 33, wherein said effect comprises an adverse effect of said electrification.

47. A method according to claim 46, wherein said adverse effect comprises blood pooling.

48. A method according to claim 33, wherein varying comprises further increasing said blood flow.

49. A method according to claim 33, wherein varying comprises reducing said blood flow.

50. A method according to claim 33, comprising receiving a manually assisted indication of a physiological parameter and wherein said varying is responsive to said manually assisted input.

51. A method according to claim 33, comprising receiving an indication of an environmental variable and wherein said varying is responsive to said environmental variable.

52. A method according to claim 33, wherein said electrification is synchronized to a

physiological parameter.

53. A method according to claim 33, wherein said electrification is synchronized to a user input.

54. A method according to claim 33, wherein said electrification is synchronized to another therapy associated with said treated tissue.

55. A method according to claim 54, wherein said electrification prevents or counteracts an adverse reaction caused by said other therapy.

56. A method according to claim 54, wherein said electrification enhances said other therapy.

57. A method according to claim 54, wherein said other therapy counteracts or prevents an adverse effect of said electrification.

58. A method according to claim 54, wherein said other therapy comprises a medication-based therapy.

59. A method according to claim 54, wherein said other therapy comprises a heat therapy.

60. A method according to claim 54, wherein said other therapy comprises an exercise therapy.

61. A method according to claim 54, wherein said other therapy comprises electrical control or activation of muscles.

62. A method according to any of claims 33-61, wherein said tissue comprises skin.

63. A method according to any of claims 33-61, wherein said tissue comprises an

internal organ.

64. A method according to claim 63, wherein said internal organ is selected from the group comprises kidney, liver, pancreas, gall bladder, brain and GI tract.

65. A method according to claim 63, wherein said electrification redistributes blood within said organ such that two parts of said organ have different blood flow levels.

66. A method according to claim 63, wherein said electrification redistributes blood between two organs.

67. A method according to claim 66, wherein said two organs do not share a secondary supply vessel.

68. A method according to any of claims 33-61, wherein said tissue comprises adipose tissue.

69. A method according to any of claims 33-61, wherein said tissue comprises a tumor.

70. Apparatus for treating using vascular control, comprising:
an electric field applicator adapted to apply an electric field to a blood vessel;
a sensor for detecting an effect of said applied electric field; and
a controller that varies said field application responsive to said detected effect.

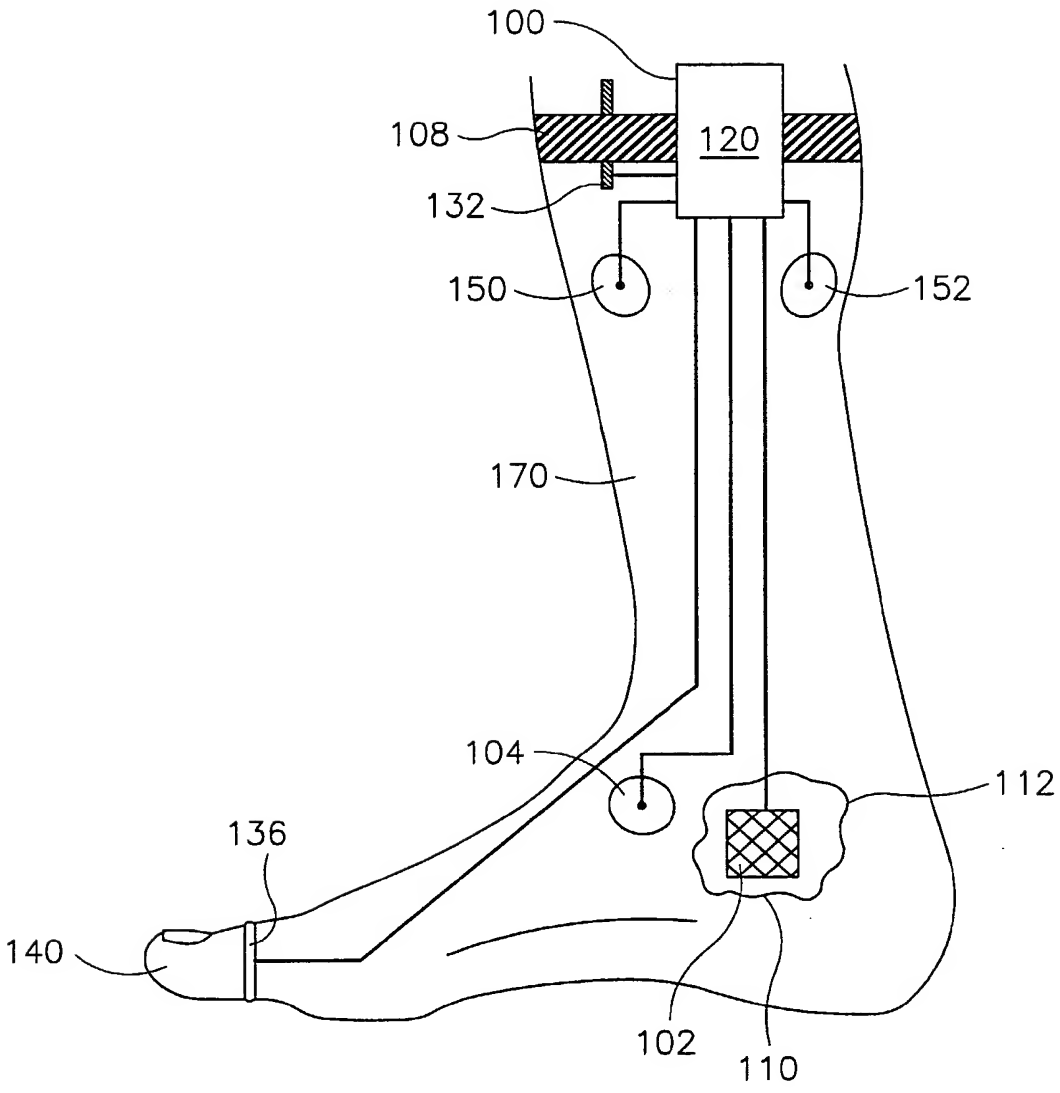

FIG.1

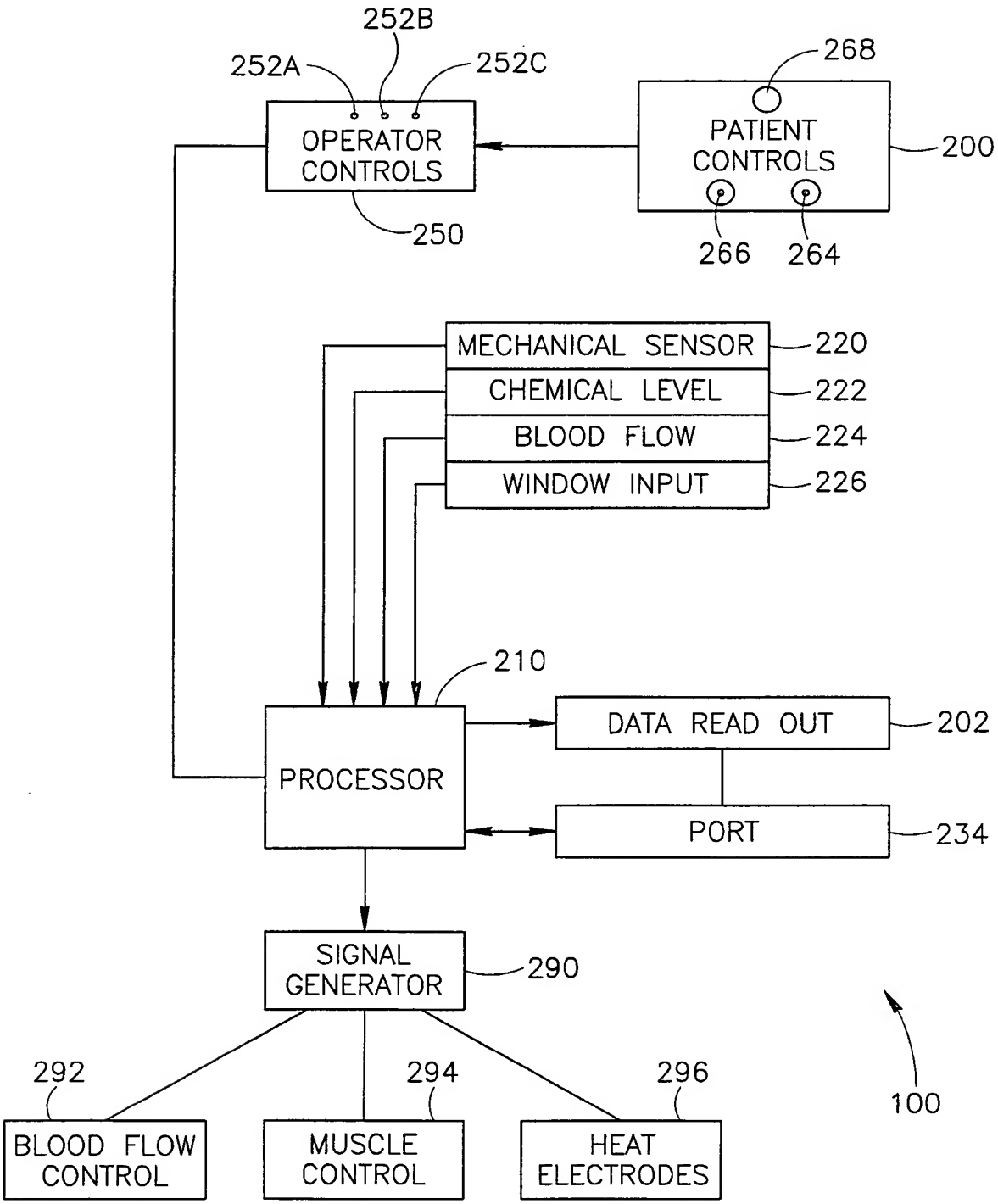
252B
252A
252C
268
OPERATOR CONTROLS
PATIENT CONTROLS
200
250
266
264
MECHANICAL SENSOR
220
CHEMICAL LEVEL
222
BLOOD FLOW
224
WINDOW INPUT
226
210
PROCESSOR
DATA READ OUT
202
PORT
234
SIGNAL GENERATOR
290
292
294
296
BLOOD FLOW CONTROL
MUSCLE CONTROL
HEAT ELECTRODES
100

FIG.2

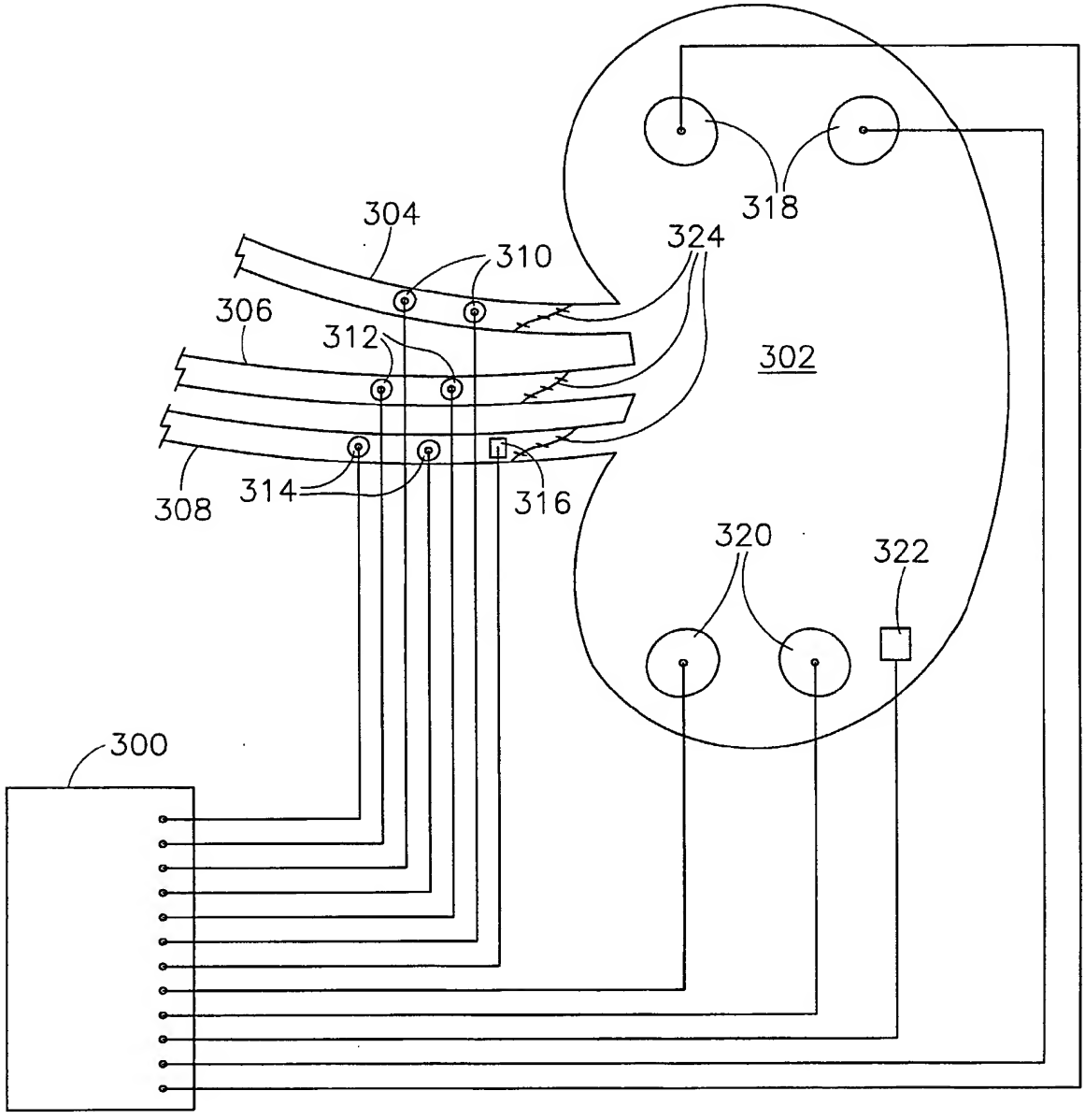

FIG.3

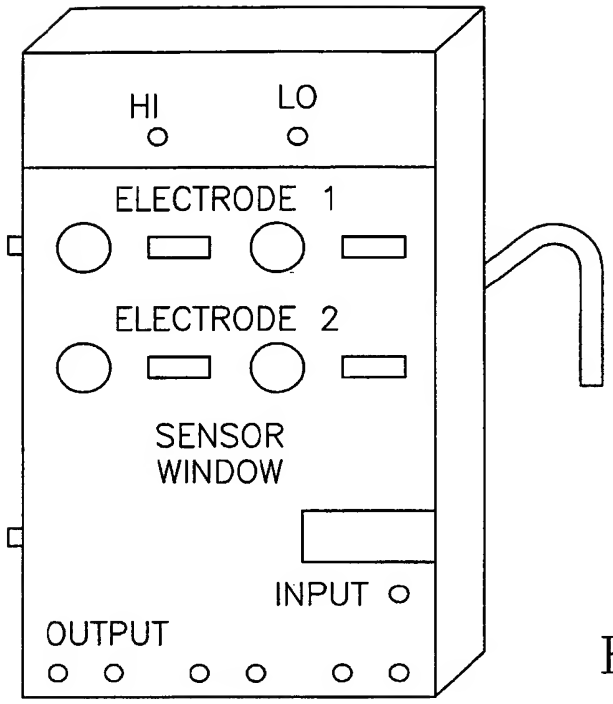

FIG.4

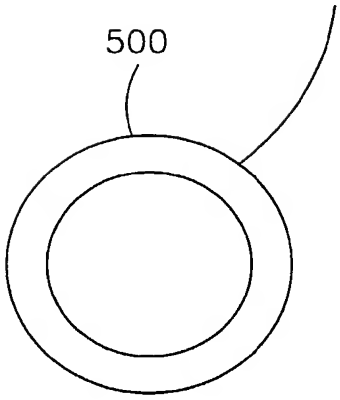

FIG.5A

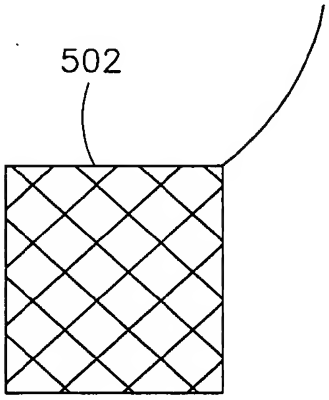

FIG.5B

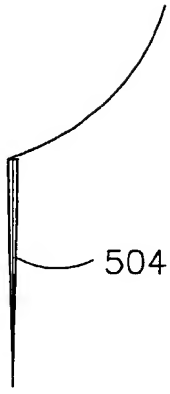

FIG.5C

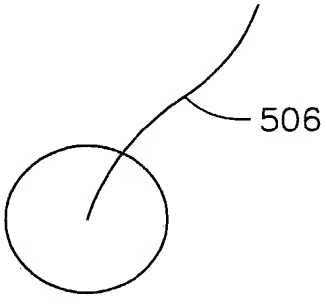

FIG.5D

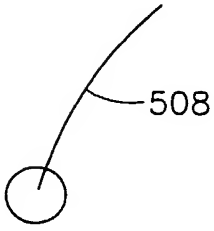

FIG.5E

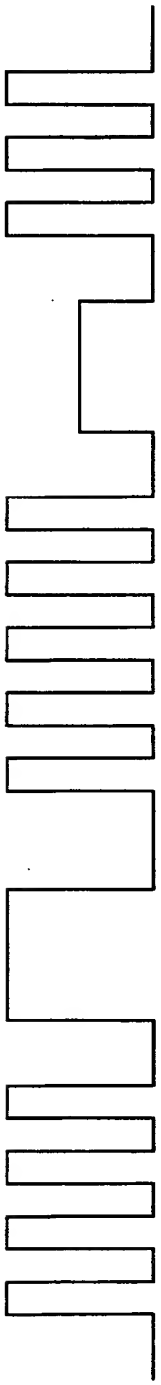

FIG.6A

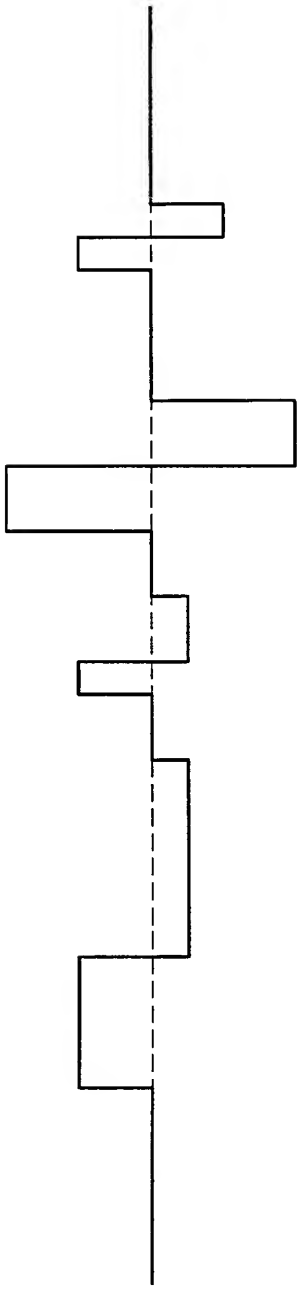

FIG.6B

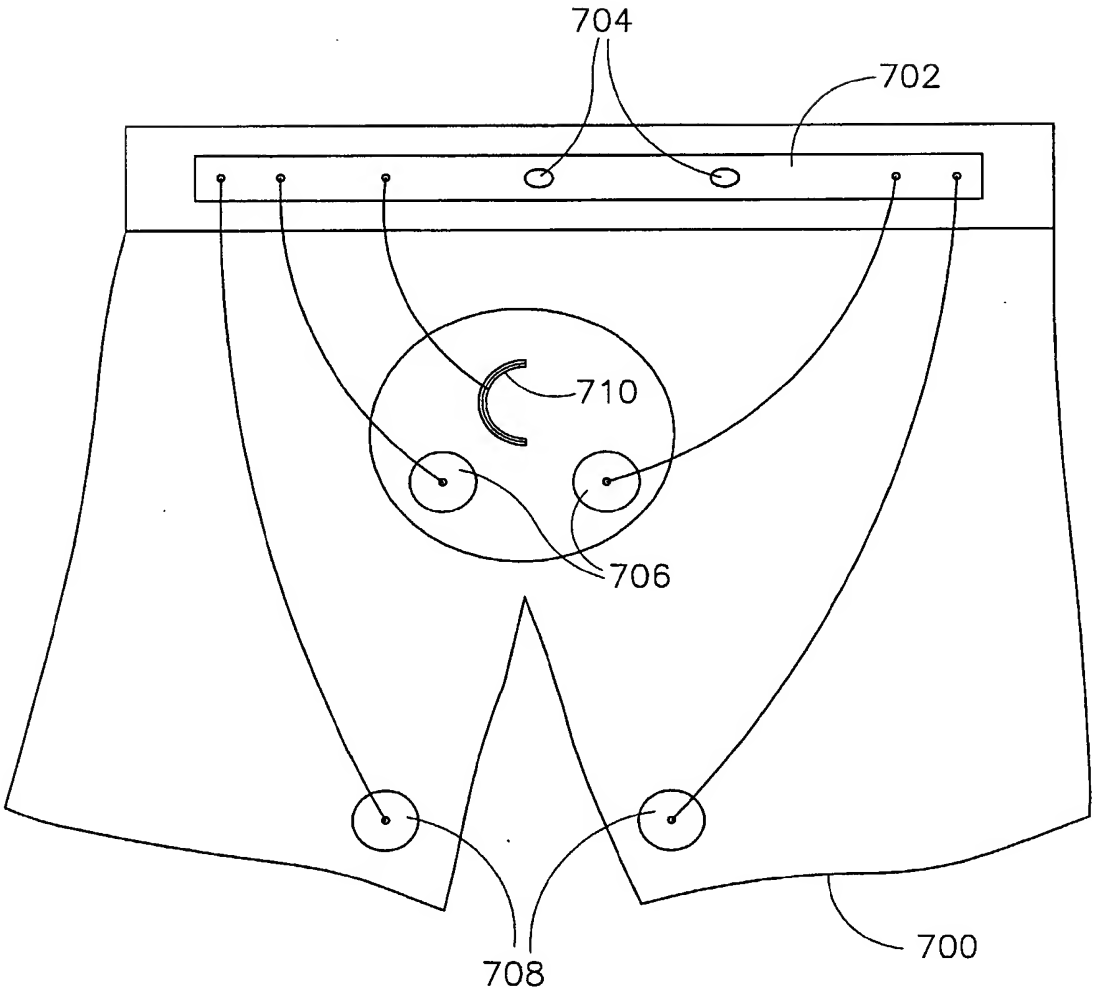

FIG.7A

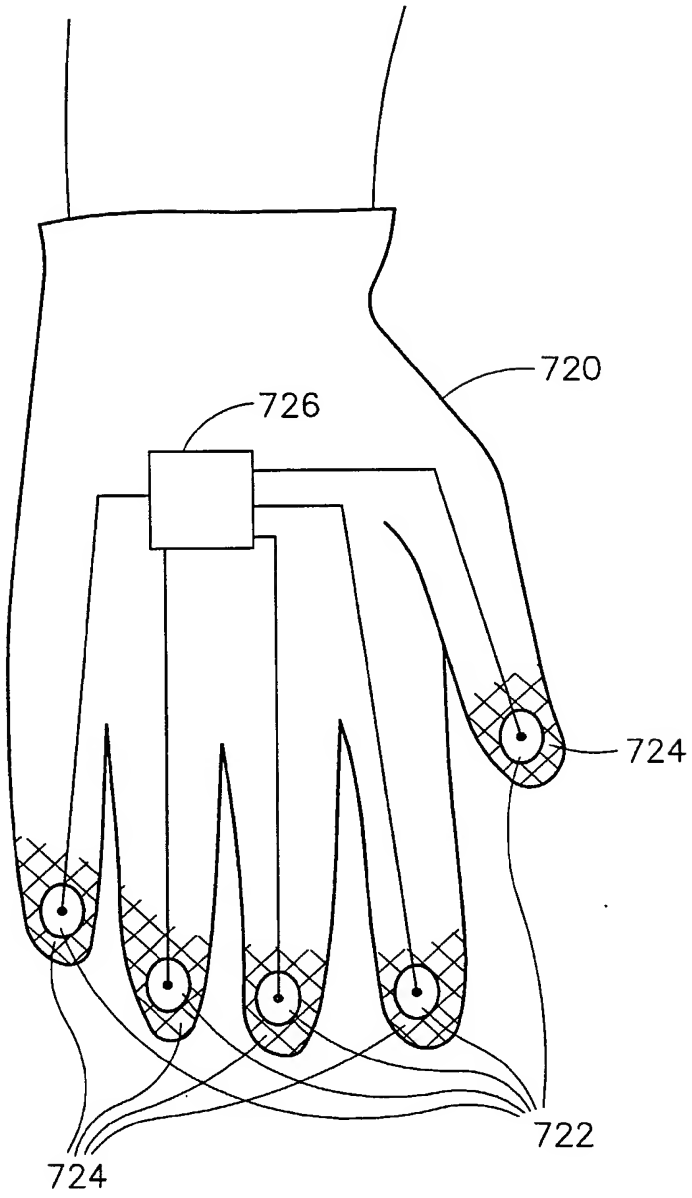

FIG.7B

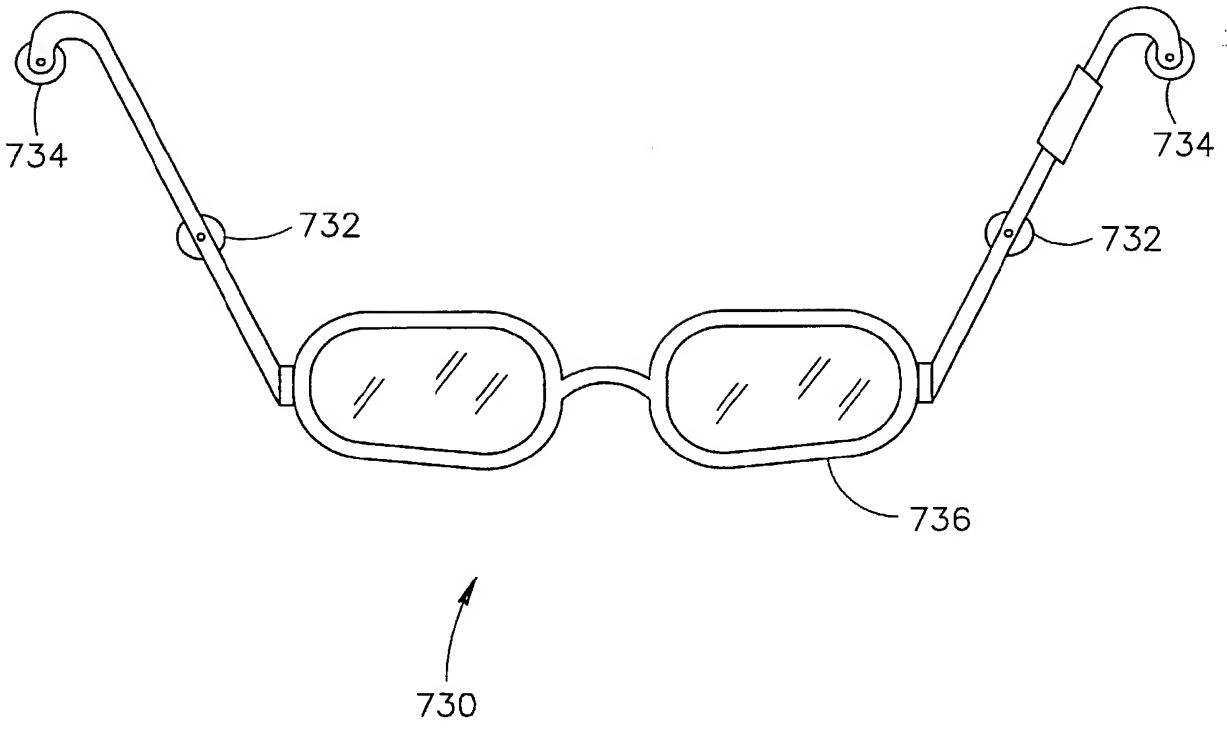

FIG.7C

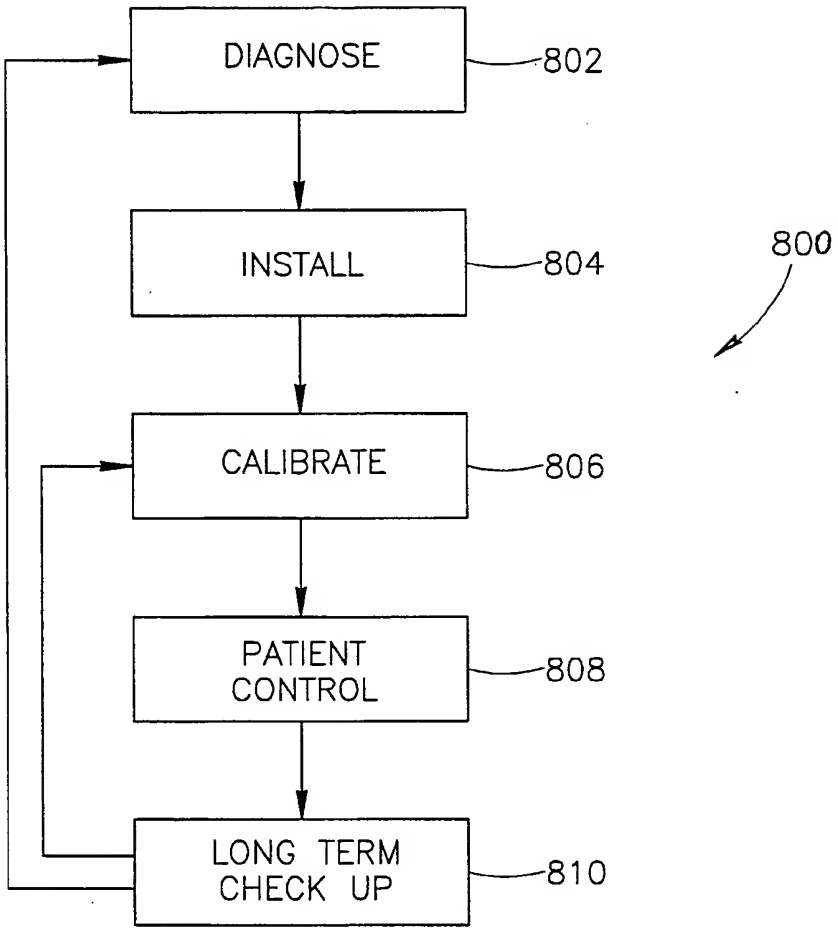
DIAGNOSE
802
INSTALL
804
800
CALIBRATE
806
PATIENT CONTROL
808
LONG TERM CHECK UP
810

FIG.8A

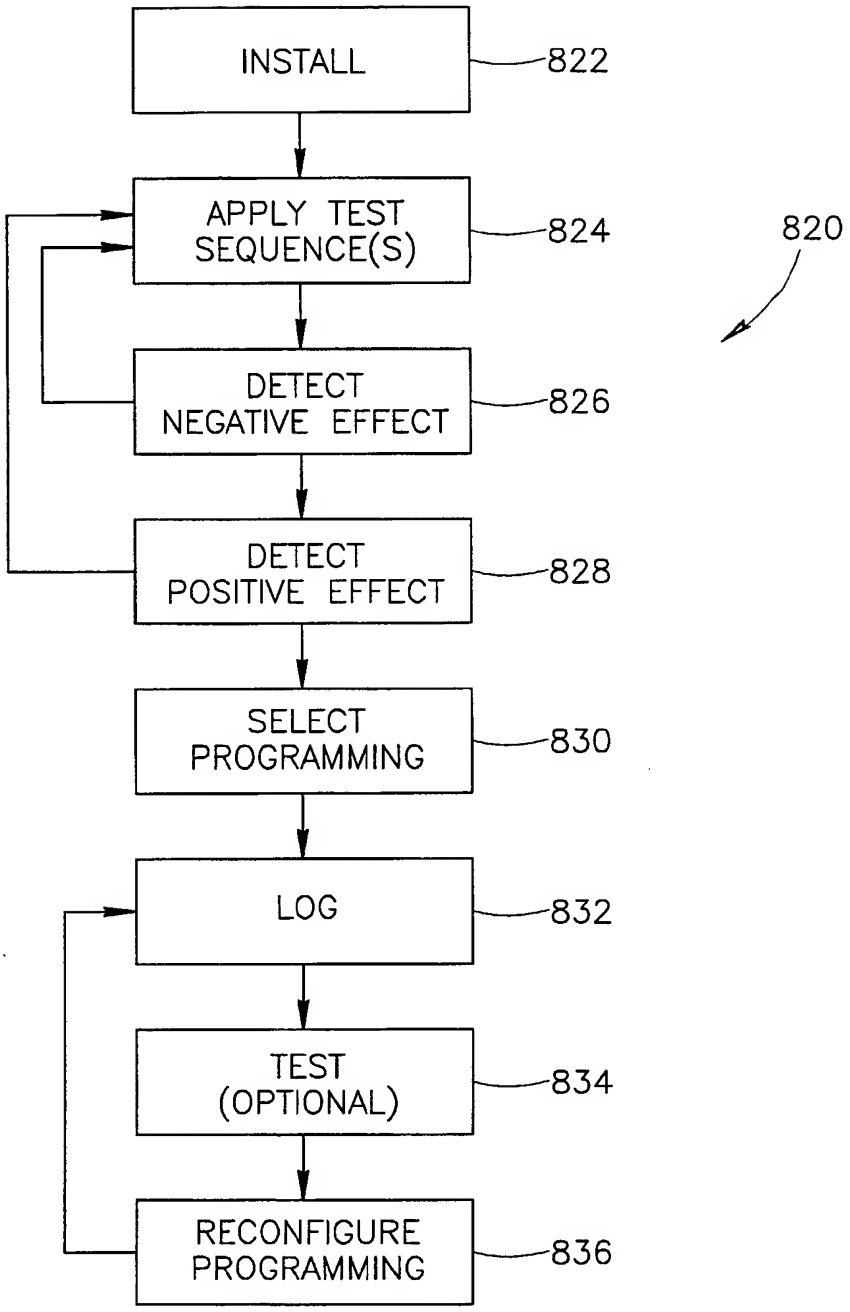
INSTALL
822
APPLY TEST SEQUENCE(S)
824
820
DETECT NEGATIVE EFFECT
826
DETECT POSITIVE EFFECT
828
SELECT PROGRAMMING
830
LOG
832
TEST (OPTIONAL)
834
RECONFIGURE PROGRAMMING
836

FIG.8B

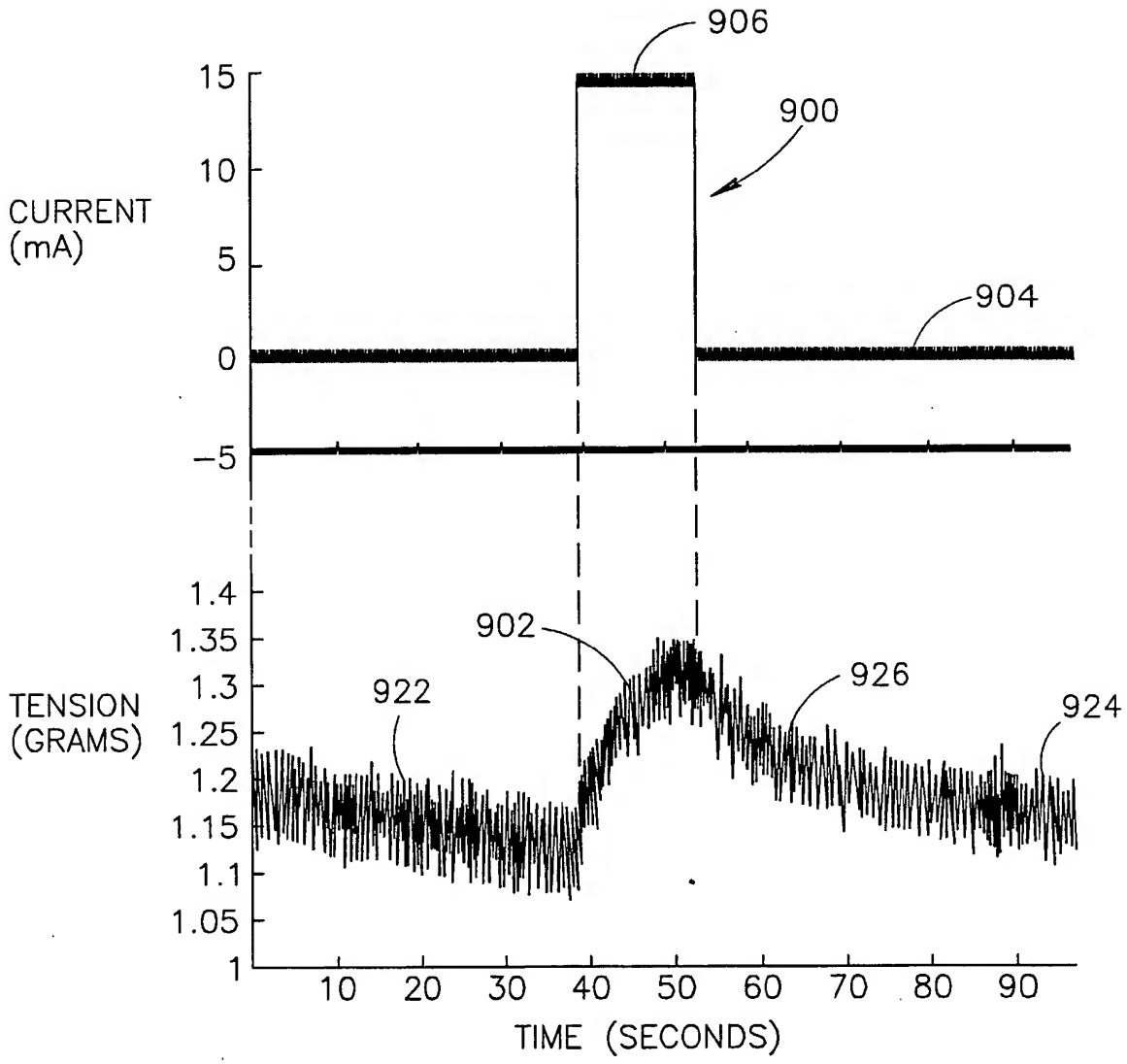
906
900
904
15
10
5
0
−5
CURRENT
(mA)
1.4
1.35
1.3
1.25
1.2
1.15
1.1
1.05
1
902
922
926
924
TENSION
(GRAMS)
10
20
30
40
50
60
70
80
90
TIME (SECONDS)

FIG.9A

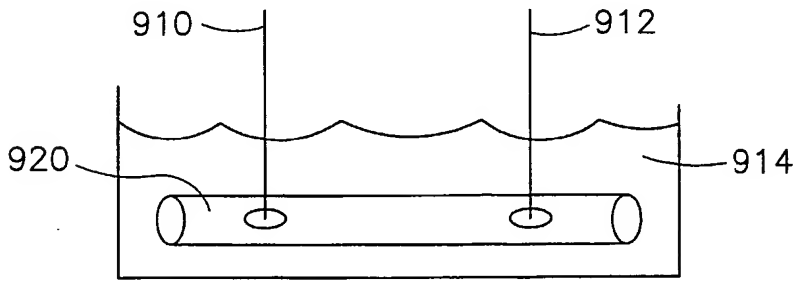
910
912
920
914

FIG.9B

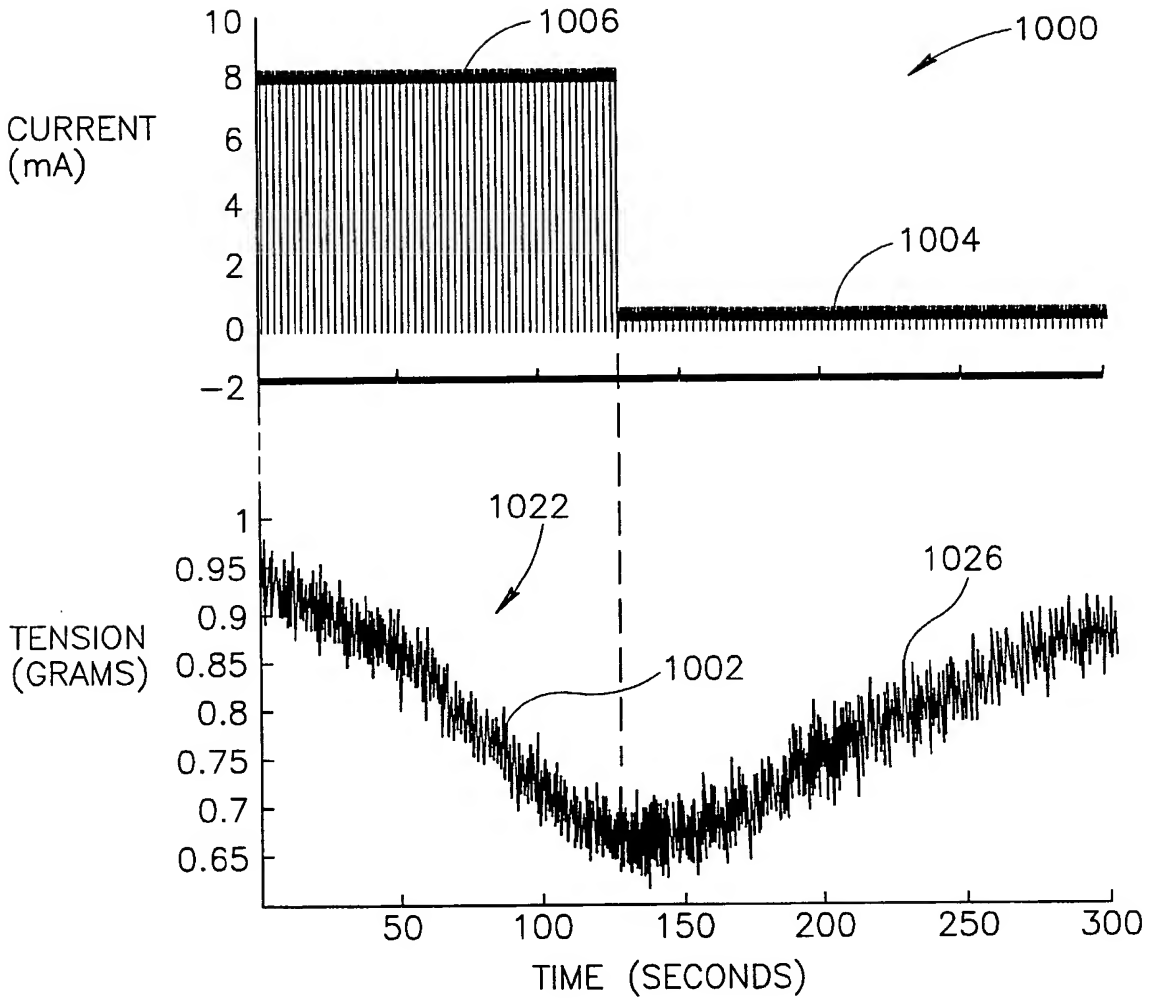

FIG.10A

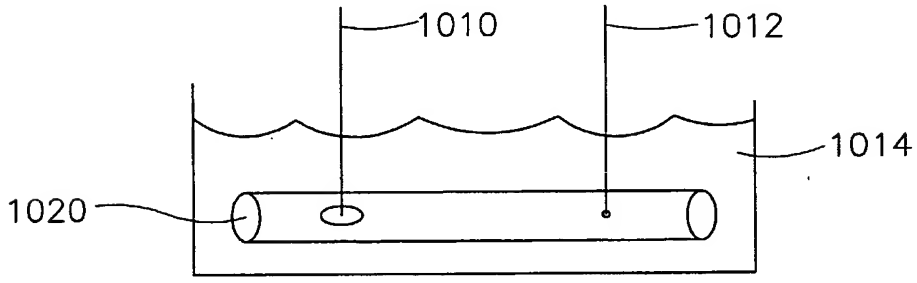

FIG.10B

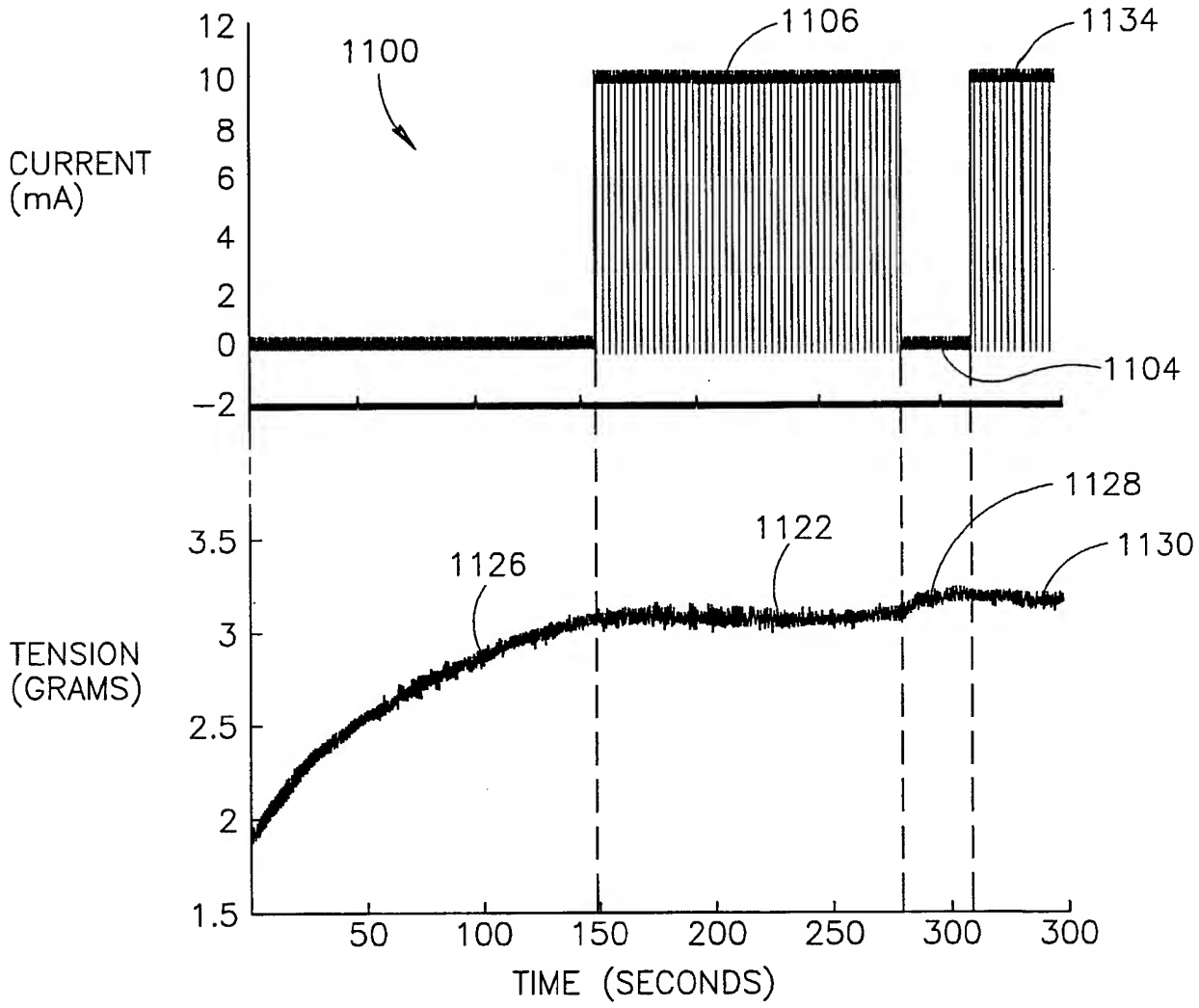

FIG.11A

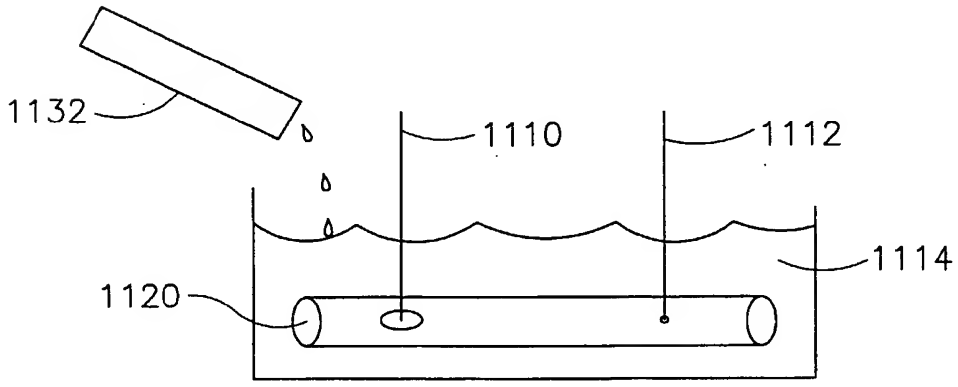

FIG.11B

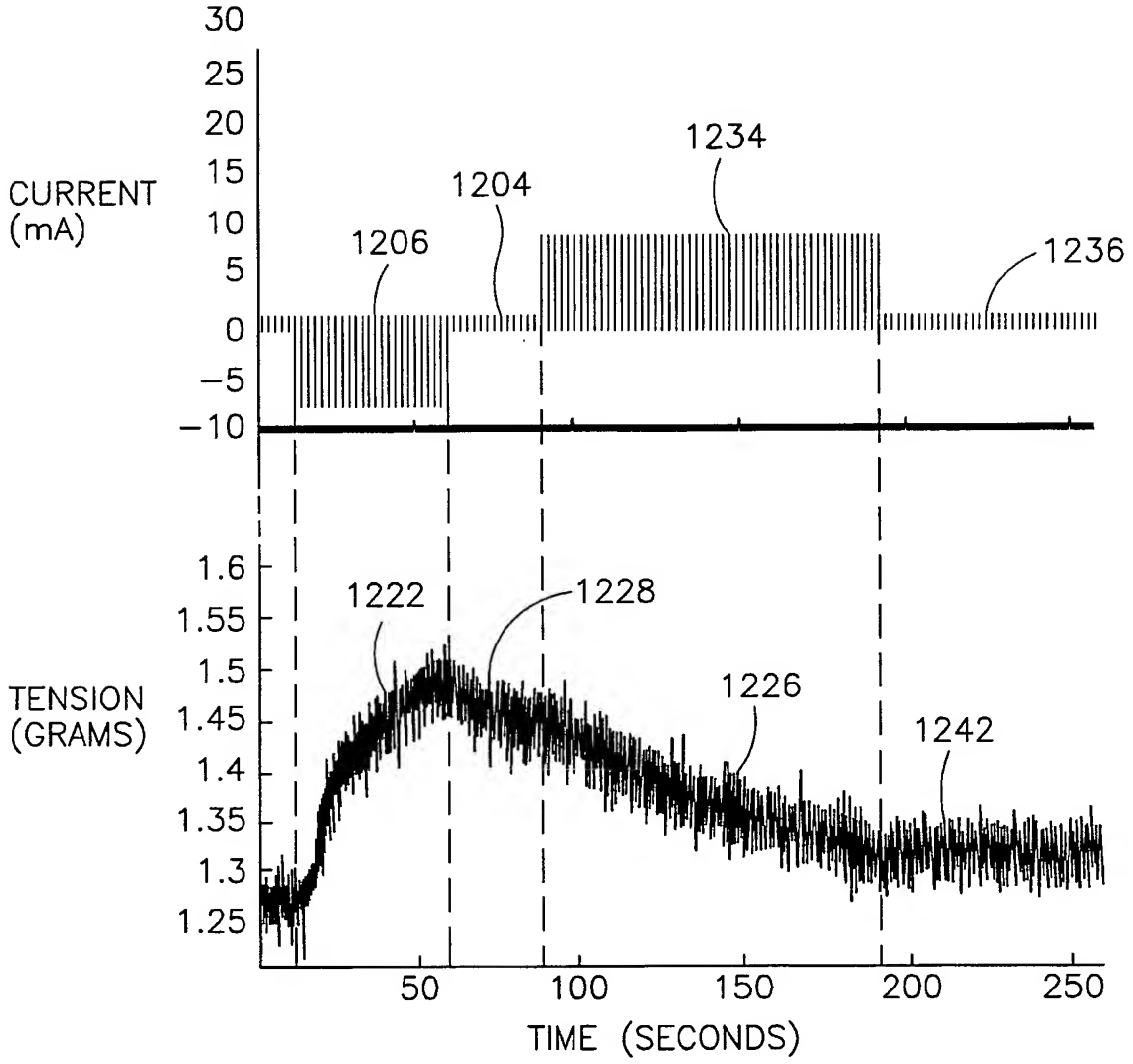

FIG.12A

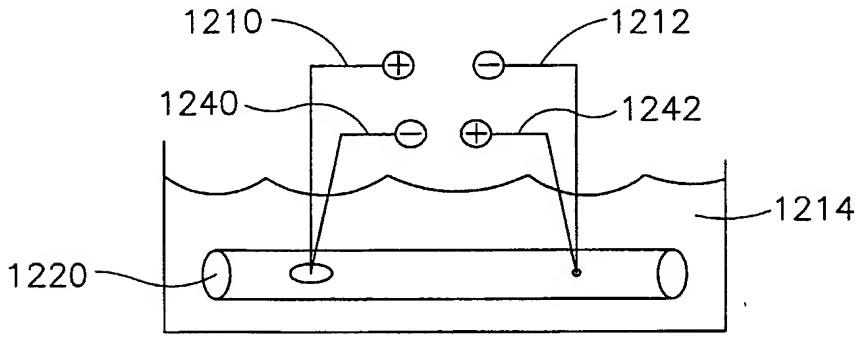

FIG.12B

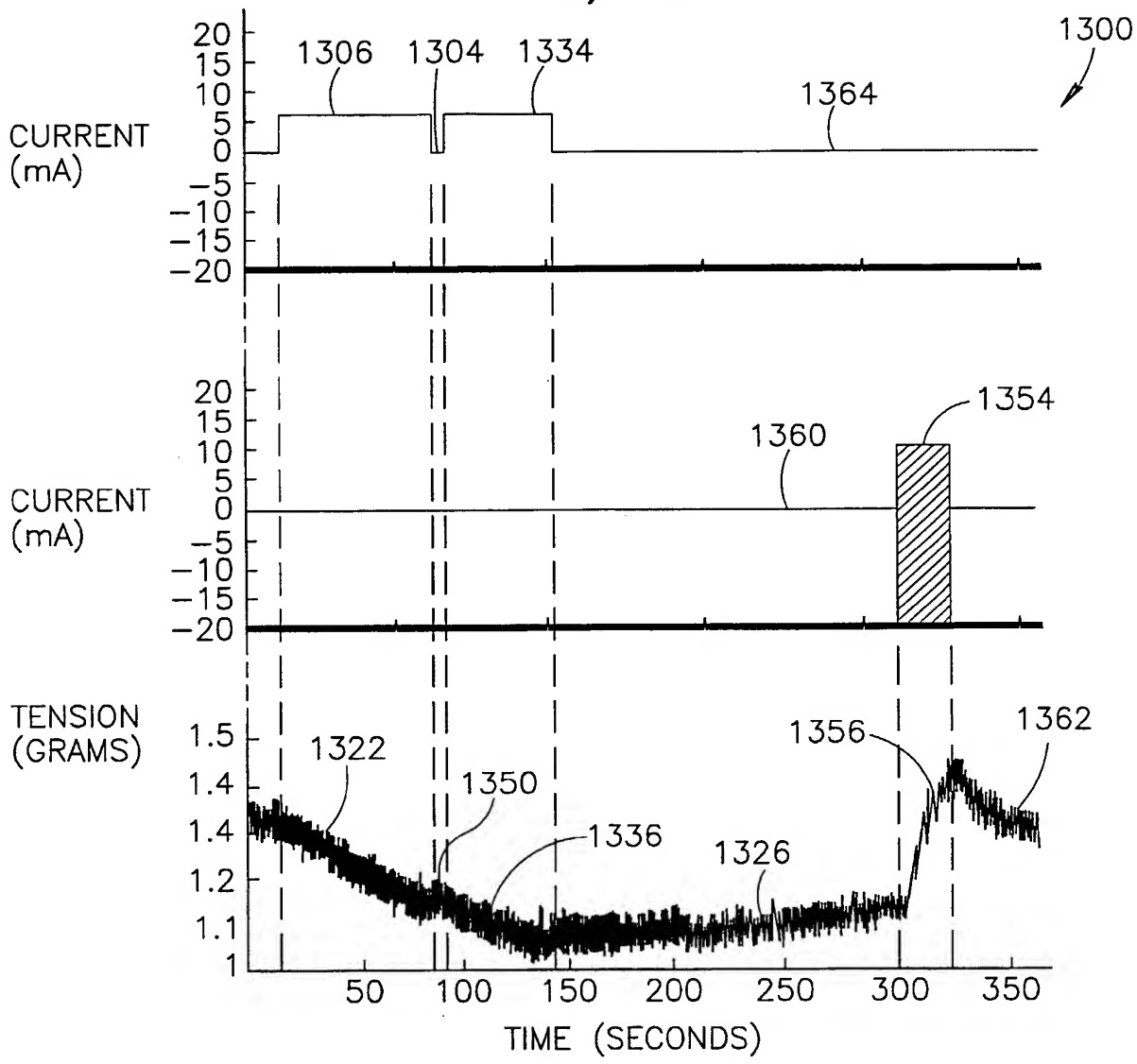

FIG.13A

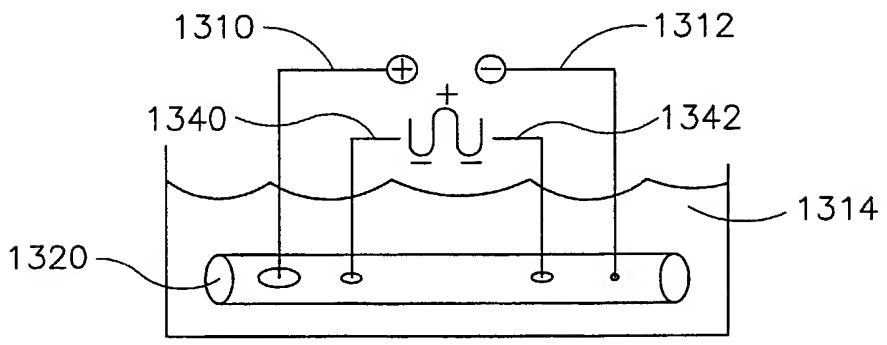

FIG.13B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL01/00056

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61N 1/05
US CL : 607/2

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 607/2, 39-51

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	US 6023640 A (ROSS) 8 FEBRUARY 2000, SEE ENTIRE DOCUMENT.	1-9, 13-15, 20-21, 33-40, 48, 59, 62

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 09 APRIL 2001	Date of mailing of the international search report 27 APR 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JEFFREY R. JASTRZAB Telephone No. (703) 308-2097

Form PCT/ISA/210 (second sheet) (July 1998)★